PRACTICAL PATHOLOGY

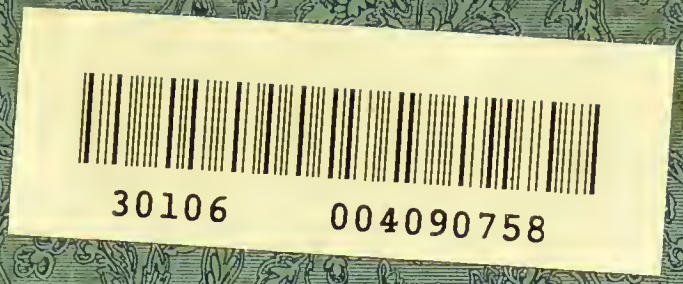
A MANUAL FOR STUDENTS

AND PRACTITIONERS

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PRACTICAL PATHOLOGY.

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A MANUAL FOR STUDENTS AND PRACTITIONERS.

LEEDS & WEST RIDING
MEDICO CHIRURGICAL SOCIETY

BY

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ETC. ETC.

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PREFACE.

WHILST there are in abundance systematic treatises upon Pathology, and the results of researches of those most eminent in the pathological world are within the reach of all, there is yet a want of a guide to the practical work involved in the study, preparation, and examination of Morbid Tissues. This want, so great as to have become almost a reproach to Pathologists, the author of this hand-book has endeavoured to supply. Though vast strides have recently been made in this branch of medical study, one of the most important bases of Clinical Medicine, the Student and the Practitioner have had very scant opportunity of thoroughly acquainting themselves with the appearances of Diseased Organs and Tissues. Acquaintance with naked eye and microscopic appearances of diseased structures is necessary for the comprehension and appreciation of recent pathological researches, and can be acquired only by a diligent use of the scalpel and microscope.

The necessity for such practical work was recognised abroad earlier than in our own country. At the present time practical teaching in Morbid Anatomy and Pathological Histology is more general than was formerly the case in our Medical Schools. The Author hopes that his work will greatly aid both Students and Practitioners in familiarising themselves with the methods and results of pathological inquiry, and that it will prove to be an adequate introduction to Systematic Pathology. It is not designed to displace so much as

to aid and supplement oral instruction in Practical Pathology, and to prepare the Student for the Lecture-room, and for the study of more systematic text-books.

The plan adopted is to follow the tissue from the body to the microscope, to describe the method of making the *post mortem* and naked eye examinations, and of preparing the various structures for microscopic investigation. The more important changes of each organ are indicated, though all the changes which occur could not possibly be considered in the space at command. In all cases the aim has been to describe at least the more important typical lesions. In as many instances as possible, illustrations, which are not mere diagrams, are added. Most of the original Drawings have been made from Sections prepared in the course of the work of the Edinburgh University Practical Pathology Class. They may therefore be accepted as representing as faithfully as possible the appearances which may be recognised by any normally intelligent and dexterous student. The copied Drawings, taken from the best sources, as far as possible are acknowledged in the descriptions.

The Author is greatly indebted to numerous writers for many of the facts adduced, but has preferred to acknowledge generally his indebtedness rather than to cumber his work with individual references. He is constrained to mention with gratitude the late Professor Sanders's Course of Pathology, and Professor Hamilton's and Professor Greenfield's Courses of Practical Pathology, on the outlines of which two practical courses the work is based. To Professor Greenfield he is indebted for much valuable assistance, especially in connection with the sections on Diseases of the Kidney and Broncho-Pneumonic Phthisis. The author has found that Professor Ziegler enunciates views similar to those of Professor Greenfield upon the Pathological Histology of Granular Contracted

Kidney and Acute Phthisis. He therefore feels it incumbent upon him to record that Professor Greenfield's investigations were completed and published in Papers and Lectures before Professor Ziegler's Pathology appeared, and that the two sections (Kidney and Lung) of the present work were already printed when the corresponding sections in Ziegler's Pathology appeared.

Such descriptions as occur of the Normal Histology of various organs are based mainly on Klein and Noble Smith's admirable work. Only such points are referred to as may prove to be of very great assistance in following pathological changes. Every student is advised to make himself thoroughly acquainted with Normal Histology before commencing the study of Morbid Tissues.

In the section dealing with Parasites, the general plan has been departed from in some measure. A few comparatively full descriptions are offered, and in addition merely a list of the more important forms.

As the work was written at intervals between the discharge of more pressing duties, the Author is prepared for many imperfections in it. He hopes there may be very few so glaring as in line 2, § 124, p. 119, where "Greenhow" appears for "Goodhart." He thanks most warmly Mr. Robert Robertson, M.B., C.M., and Mr. Mason, for the very full Index which they have compiled; Mr. J. Tatham Thompson for many of the Drawings; his Wife, Dr. Bendall, and Messrs. W. E. Hoyle, M.A., R. J. Harvey-Gibson, M.A., Chas. Kennedy, M.B., C.M., W. B. Mackay, and R. Muir for Drawings; Messrs. C. W. Cathcart, F.R.C.S. (*vide* Fig. 57), and W. O. Williams, M.R.C.V.S. (*vide* Figs. 135 and 136), for the loan of preparations from which Drawings have been made.

G. S. W.

EDINBURGH, *October* 1, 1883.

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PRACTICAL PATHOLOGY.

CHAPTER I.

POST MORTEM EXAMINATION.

1. Instruments required.—

(*a.*) A couple of scalpels, such as are supplied in the ordinary dissecting cases.

(*b.*) Two or three strong "section" knives, which should be strong enough to be used as cartilage knives. The handle must be strong and thick enough to be grasped firmly in the palm of the hand. The blade also should be stout, with the belly curved and sharpened up to the point, which may with advantage be slightly rounded off.

(*c.*) Two curved bistouries; one probe-pointed, the other sharpened up to the point.

(*d.*) A hollow ground razor (Heifor's army razor), or better, a Valentine's knife, for cutting thin sections of tissues.

(*e.*) A long thin-bladed knife, about one inch broad and ten or twelve inches long, for making sections completely through the various visceral organs. This is especially necessary for cutting into the brain, but one rather shorter, though of similar make, is frequently used for cutting into the other viscera. For the first incision into the brain a thin narrow knife, about one-third to one-half inch wide, and ten or twelve inches long, is also exceedingly useful.

(*f.*) Two pairs of dissecting forceps.

(*g.*) Two pairs of double hooks with chain—these hooks should always be well blunted—and a couple of copper spatulae.

(*h.*) Two pairs of scissors; "one pair large, having one blade with the point rounded off, the other sharp; the other pair small, one blade probe-pointed, the other sharp-pointed."

(*i.*) A pair of intestine scissors, with a long curved and blunt-pointed blade, and a shorter square-ended blade which closes behind the curve, so that the curved blade is never cut out of the bowel.

(*j.*) A blowpipe, preferably with a stop-cock.

(*k.*) Several probes, of different sizes.

(*l.*) A small bone-saw, with a strong back and fine teeth, well set.

(*m.*) A mallet and steel chisel, in the shape of a capital T; the blade and cross-piece should each be about 6 inches in length, and the blade may be made with a guard at a distance of about one-third of an inch from the point. This guard is of use when the skull-cap is being removed, but it interferes with the use of the chisel for other purposes, such as taking out the spinal cord, so that when the guard is adopted a second straight steel chisel should be added to the list of instruments.

(*n.*) One pair of strong bone-forceps, the two handles of which should be at least half an inch apart, at the end away from the blades, when they are forcibly gripped in the hand.

(*o.*) Half a dozen curved needles, of different sizes, and some strong twine.

(*p.*) A pair of caliper compasses, with graduated cross-bar. A yard or metre tape or steel band measure finely graduated. A series of graduated cones, for measuring the diameter of various orifices, from one-tenth inch to three inches diameter. A large well-graduated glass measure of about twenty ounce capacity. A smaller graduated beaker-shaped one ounce glass measure.

(*q.*) A pair of scales, with weights from one-quarter ounce to about ten pounds.

(*r.*) Blue litmus papers and turmeric papers. A weak solution of iodine, made by adding one drachm of tincture of iodine to eight or ten drachms of water.

(*s.*) A good magnifying glass and a compound microscope with accessories, such as slides, cover glasses, a couple of needles in handles, a small phial of neutral solution (three-fourths per cent. solution of common salt in distilled water). (See Chapter II.)

Of these instruments, those for cutting must all be perfectly clean and sharp, as nothing is so likely to interfere with the accuracy of the results of an examination as a set of blunt instruments—except want of method. It is needless to say, however, that many *post mortem* examinations have to be made without the aid of many of the above instruments (and the lack of some of them should never be put forward as a reason for not making an examination), but these, or substitutes for them, should be obtained when possible.

2. In the *post mortem* theatre of an infirmary all the requisites for sponging the body, washing out cavities, &c. are provided; but where the examination has to be conducted in a private house, the following matters should be attended to beforehand :—

A good firm kitchen table is to be placed in the room where the cadaver is lying. This room should be well lighted, and as large as possible. Over the table is spread a piece of stout Mackintosh. A couple of wash-hand basins must be procured, two empty pails, a plentiful supply of water, hot and cold, a bottle of one to twenty carbolic acid watery solution, some turpentine, and some carbolic oil, one to five.

In addition, three or four sponges, a piece of soap, and several towels, are absolutely essential.

The hands of the operator should be thoroughly washed with warm water and turpentine, and after that a stream of cold water allowed to run over them. They are then to be anointed thoroughly with the carbolic oil. From time to time during the section the stream of cold water should again be run over the hands. When all is completed, wash thoroughly, first with cold and then with warm water, soap, and turpentine, and when the hands are thoroughly clean, pour some of the carbolic lotion over them, and allow it to dry, almost, before wiping.

If the skin is cut, scratched, or pricked, the hands should be at once cleansed, and pure nitric acid or strong acetic acid applied to the abrasion, which should then be covered with good waterproof plaster or an indiarubber finger cap.

3. Before the section is commenced a careful note should be made of the time at which the patient died, the interval (in hours) that has elapsed between the death and the examination of the body, and the temperature. This is "of considerable importance," as upon the time that has elapsed depends the condition or state of preservation of the organs and the degree of *post mortem* change, and it enables the observer in many cases to decide whether certain changes are *ante mortem* or whether they have come about subsequent to the death of the patient.

4. A careful and systematic examination of the external appearances of the body must next be made, and the results noted down in as clear and accurate a manner as possible. This may be done in the following order :—

Name, age, and sex (for reference); height (from vertex of the head to sole of the foot, in a line with the external maleolus); circumference around the shoulders; circumference of skull around frontal and occipital protuberances (in the case of a child the shape of the cranium, the various diameters, and the condition of the sutures and of the fontanelles should also be given); the amount of adipose tissue, or apparent state of nutrition of the body; the muscular development; and the shape and appearance generally of the head, thorax, and abdomen.

Next note the colour of the various parts of the body. Such parts as are reddened or otherwise discoloured should be firmly pressed with the fingers, and then examined to see whether the colour still remains *or not*. These discoloured patches should also be incised and the colour of the tissues and the condition of the small vessels noticed. A careful search must be made for abrasions, extravasations of blood, bed sores, ulcers, or any other evidences of a diseased condition, or scars, wounds, &c. on any part of the body, and the appearance, size, and position of these recorded.

Determine what degree of *post mortem* rigidity still remains in the various muscles of the body. Observe the eyelids, the tension of the eyeballs, the appearance of the cornea, and the relative size of the pupils. Examine the various orifices of the body—the nose and ears for discharges of any kind, and for foreign bodies which may have become impacted ; the mouth, about which should be noted the colour of the lips, the appearance and position of the teeth and of the lower jaw, and the relation of the tongue to these. Here also look for foreign bodies, and in the fauces and larynx. The organs of generation are now to be examined for any abnormality or growth. (In the child it should be noted whether the testicles have descended or not.) The anus is to be examined in a similar manner for growths, scars, or fissures. In addition to the above it should be noted in the case of a child whether the anus is perforated or not, the condition of the umbilicus and the umbilical cord, the presence or absence of *vernix caseosa*, and the condition of the various epiphyses, especially of that at the lower end of the femur, which is to be gradually cut away in thin slices.

5. In making all *post mortem* examinations it is necessary to have certain well defined rules of procedure ; and although it will be found that in a small minority of cases these rules cannot be adhered to in their entirety, they nevertheless form a basis on which to work regularly and methodically. Any one who will take the trouble to examine the various sets of rules adopted by eminent pathologists will find that they are mostly based upon Virchow's method—a method which, with more or less modification, has found almost universal favour. In the following short *resumé* of the various processes to be gone through there is nothing original ; it is an outline of a system of examination which has been found to be exceedingly convenient, and at the same time very thorough. It is based upon that given by Virchow.[1]

6. Lay it down as a cardinal rule that in all cases where possible *all* the cavities of the body are to be examined, and also that they

[1] Those who require a full and accurate description of the manner of conducting medico-legal sections should consult Virchow's "Method of Performing *Post Mortem* Examinations, with Special Reference to Medico-Legal Practice." Translated from the German by Dr. T. P. Smith.

are to be examined in a regular order (head, thorax, abdomen), which order should be adhered to, unless there be sufficient reason for departing from it. In certain cases the abdomen or the thorax may be opened and examined first; when, for instance, there is very good reason to suspect some grave lesion or lesions in the viscera contained within one or other of these cavities, and where the removal of some of the organs may disarrange the relative positions of the diseased parts. In such cases it is necessary to depart from the regular order; otherwise, it is necessary to keep to the plan as closely as possible.

Before opening the head, however, it is well to open the other cavities, and make a preliminary examination of certain of their contained viscera. This may be done as follows :—

7. Stand on the right side of the body, and with a strong sharp knife, held in the palm of the hand, make a single incision through the skin, fasciæ, and muscles, commencing at the upper border of the sternum, passing around the umbilicus, and extending to the pubes. This incision should not be carried deeper than the subperitoneal tissue. At one point, a little way below the ensiform cartilage, carefully dissect through the peritoneum; pass the fingers of the left hand through the opening so made; raise the abdominal wall, and complete the incision by cutting from within outwards, so as to avoid injuring any of the organs which are situated near the surface in this position. Examine the cut surface of muscle, and note any peculiarity; then make a careful search for any adhesion; should such be present, note its position before disturbing any of the organs. At the same time notice the relative position and colour of the various viscera. (This should be done as soon as the body is opened, and before oxidation of the colouring matter of the blood can be brought about by the presence of air.) It is to be remembered that in all cases either the external surface or a cut surface must be examined at once, and the colour noted, though these surfaces are also to be examined later, when the blood has become oxygenated, and has assumed the bright red colour commonly associated with arterial blood. The position of the diaphragm is to be carefully noted; and, lastly, any fluid contained within the cavity is to be re-

moved, measured, and examined, and any sign of inflammation, lymph, foreign body, or tumour is to be accurately observed and localised. The examination of the abdomen must for the present be carried no further, but a partial examination of the thorax must next be made.

8. Remove the sternum thus :—With a strong cartilage knife cut through the sterno-costal cartilages as near to the end of the ribs as possible, and cut downwards, outwards, and backwards, following the line of the attachment of the ribs to their cartilages, commencing with the second rib and passing down to the ninth, the line of incision gradually curving outwards, this curvature becoming greater as the floating ribs are reached and cut through. If care is taken to carry the knife in an oblique direction, the cartilages are cut through with comparative ease, but unless this direction be taken, it is often a matter of very great difficulty to divide these tough cartilaginous structures. In certain cases the cartilages have become ossified, and it is found impossible to divide them with a knife. Then, as the object is to get a very free access to the chest cavity, the best plan is to divide the ribs with bone-forceps at some little distance from the cartilages. Whichever method is adopted, great care must be taken not to injure the pleural sacs. Having separated the ends of the ribs, raise the sternum with the left hand, and carefully cut away the bone from the soft tissues beneath, making one cut downwards (towards the feet), to separate the diaphragm from its attachments to the lower part of the sternum, make two lateral cuts above the curve already described, and then pass the knife upwards to the manbrium. Raise the sternum still higher, introduce the saw, and notch the bone immediately below the level of the first rib, when it may be readily broken and turned back. This is, as a rule, all that is necessary to expose pretty fully the thoracic viscera ; the first rib and the clavicle are still left, and the disfigurement of the body is not very great. Sometimes, however, where a more complete dissection of the neck has to be made, the mesial incision must be carried up to the chin, after which the cartilage of the first rib (which is very frequently ossified) must be divided, and the clavicle disarticulated. To divide the first costal cartilage the knife must pass

a little further outwards than in the case of the second rib, and on account of the frequent ossification it is often necessary to use the bone-forceps even when the other cartilages have been readily divided with the knife. According to Virchow, "The best way to proceed is to insert the knife with its edge looking upwards and forwards, under the cartilage of the first rib, below its inferior border and then cut upwards and forwards." Divide the sterno-clavicular ligaments, and turn the sternum backwards. The next step is to open the pleural sacs, notice the position, state of distension, colour, and general appearance of the lungs, pass the hand between the two pleural surfaces, and make sure of the presence or absence of adhesions, or of any foreign body. Carefully remove, measure, and examine any fluid which may be present, just as in the case of the abdomen. Do not for the present attempt to remove the lungs, but note carefully the condition of the mediastinum, the size and appearance of the thymus gland, and the appearance of the vessels outside the pericardium; then open the pericardial sac, and again notice points of adhesion, appearance of surfaces of the heart and pericardium, after removing any fluid which may be in normal quantity, or in greater or less excess; and lastly, note the state of distension or contraction of the various chambers and vessels of the heart. Not until this point is reached can we commence to remove any of the viscera, as such removal is necessarily accompanied by a considerable loss of blood, which drains away from the heart, and so may alter very considerably the state of distension of the cavities of that organ.

9. From this point the dissection passes regularly downwards, commencing with the head and neck, going into the thorax, and then down to the abdomen. *Head.*—An incision is to be made transversely over the vertex of the skull from ear to ear, cutting from within outwards after transfixing the skin, so as to cut away no more hair than is absolutely necessary, and also to keep the knife in good order. If this is not done, the hair should be carefully parted before-hand along the line of incision. Reflect the skin over the occiput and over the forehead, exposing the occipital protuberance and the eminences over the frontal sinuses. Then carefully examine the soft tissues

and the outer surface of the bones for any abnormal appearances; carry the knife round the skull at the level above indicated, and divide any adherent soft tissues, the temporal muscles, &c., and saw through the outer dense layer of bone in this circular direction, taking care not to allow the saw to pass through the whole thickness of the skull. To complete the separation of the skull-cap use the mallet and steel chisel, breaking through the inner table, unless a fracture of the bones of the skull is suspected, in which case, as is evident, it is better to use the saw more freely, even at the risk of injuring the membranes, or even the brain itself. Then using the cross-bar as a lever, detach the skull-cap from the subjacent membranes. In most cases this is readily enough managed, but in persons who have suffered from chronic alcoholism, or who have had hard knocks to bear, it is not so easily accomplished, owing to the presence of adhesions. In children, too, where the bones are still growing rapidly, there is almost invariably adhesion of the skull-cap to the dura mater beneath. In such cases it is better to combine the removal of the bony cap with the next stage. Where the skull-cap can be detached the appearances of the surface of the dura mater are to be noted, and the superior longitudinal sinus is to be laid open and examined.

Next make a small opening into the dura mater on each side, just above the bony margin, and pass in at these openings a curved probe-pointed bistoury, carrying it to the mesial line on both sides, backwards and forwards, so as to thoroughly divide the membrane; then with a pair of scissors cut through the attachment to the crista galli, and draw back the membrane, falx cerebri and all, from the surface of the brain, leaving it attached at the position of the meeting of the sinuses. Examine its inner surface, the exposed arachnoid and pia mater, and then proceed to remove the brain.

With the fingers of the left hand draw back the frontal lobes, and carefully detach the olfactory bulbs from the cribriform plate with the handle of a scalpel; then, passing the fingers gradually further and further back, so as to support the brain, divide the optic nerves and the internal carotid vessels with a sharp scalpel as near their bony channels as possible, and detach the pituitary body from its fossa. Passing backwards, divide the third nerves, the fourth pair as

they lie in the margin of the tentorium cerebelli, and the sixth nerves, which are divided along with the tentorium. In the same manner the fifth and seventh are cut with the sharp bistoury, which is further carried along the margin of the tentorium, freely dividing that membrane at its point of attachment to the petrous portion of the temporal bone. Cut through the eight and ninth nerves, then, with a long sharp-pointed bistoury, divide the cord as low down in the canal as it is possible to reach, and carefully tilt the brain backwards from the cranial cavity with the right hand, supporting it beneath with the left. Lay it aside until the examination of the inner surface of the dura mater at the base of the skull is completed.[1] Here look for any altered conditions or new growths. Slit open the various sinuses, and note their contents (as the state of distension of the right auricle has been already observed, it is not a matter of very great importance that the escape of blood should be prevented), examine the various vessels at their points of entrance to the skull, after which the dura mater may be detached, and the bones at the base of the skull examined, especially the petrous portion of the temporal bone.

10. Weigh the *brain*. Then dissect it. In making this dissection it is necessary (as in dissecting all the viscera) to have two ends in view:—*1st*. To make as complete a naked eye examination as possible; *2d*. To have the organ so cut up that it will be possible to replace each separate part in its proper position, to enable the operator to examine the organ as a whole, or to take any small portion from a precise given area with certainty. These ends may be attained in one of several ways, but it will be well here to give two methods, by either of which this examination may be made thoroughly and well. (In either of these methods, Virchow's cardinal rules for the attainment of the object in view should be constantly borne in mind. They may be summed up in the following:—(1.) Make bold, free incisions by traction through the thickest, broadest, and longest part of the organ: (2.) Leave the fibrous covering of the

[1] To support the brain on the table, twist a cloth into a roll, make a circle with it, in the concavity of which the organ may rest.

organ, some of the vessels, or some of the parenchyma of the organ, to bind one edge of the sections together.)

(*a.*) Virchow's method slightly modified.—With a long, thin, narrow-bladed knife cut horizontally from within outwards into the hemisphere, just above the level of the corpus callosum, leaving the upper part of the brain attached to the lower, by the pia mater only, at its outer margin; make a similar incision into the opposite hemisphere. Then examine the lateral ventricles before any excess of fluid has time to escape, by cutting vertically down into the corpus callosum at a distance of one-sixteenth of an inch from the mesial plane, until at a depth of one-eighth of an inch the knife comes directly into the lateral ventricle. This incision is to be extended both backwards and forwards for some distance, in order to expose the "body" of the ventricular cavity (note the quantity of fluid that escapes). Then divide and subdivide several times the upper portion of the cerebral hemispheres already turned outwards. Here, again, always cut from within outwards, and leave the pia mater intact to hold together the wedge-shaped lamillæ. To open into the anterior horn of the ventricle cut horizontally into the frontal lobe a little below the level of the body of the cavity, removing the brain substance above the incision. The posterior horn is opened into in a similar fashion, the horizontal incision, however, being made in a plane about three-quarters of an inch lower.

Now separate the pons, medulla, and cerebellum from the brain proper by cutting towards the mesial line in a plane the anterior border of which is just in front of the pons, the other border lying immediately behind the posterior of the corpora quadrigemina. A similar incision is made from the opposite side, when the cerebellum, &c. may be removed, and examined later.

"Having determined the contents of the lateral ventricles," says Virchow, "the state of their walls and venous plexus, and the condition of the septum, the latter

is taken hold of with the left hand, close behind the foramen of Monro, the knife is pushed in front of the fingers through this aperture, and the corpus callosum cut through obliquely, upwards and forwards, when all these parts (corpus callosum, septum lucidum, and fornix) are carefully detached from the velum interpocitum and its choroid plexus. After these two latter have been exposed, we have to examine the state of their vessels and tissue. Then the handle of the scalpel is passed from the front under the velum, which is thus detached from the pineal body and corpora quadrigemina, the state of these parts is determined, and the third ventricle exposed."

Then open into the aqueduct of Sylvius by making a verticle incision through the corpora quadrigemina. The corpora striata and optic thalami are further examined by means of numerous incisions, "whose common starting-point is the peduncle of the cerebrum. However great the number of these incisions may be—and it is necessary here to make numerous cuts—the relationship of the parts may always be closely preserved in consequence of the connection between each separate portion and the peduncle of the cerebrum."

Cut through the peduncles of the cerebellum, after which make free incisions into this organ in the positions already mentioned (*i.e.*, to get sections having as large a surface as possible).

Treat the pons, medulla, and upper part of the cord in a similar manner, the transverse incisions to be at intervals of about from one-eighth to one-quarter of an inch, the pia mater and dura mater being left uncut on the anterior surface to bind the sections together, and keep them in position.

In some few cases, as, for example, in the brains of hydrocephalic children, where there is great distension of the ventricles, it is sometimes found convenient to do the first part of the dissection into the ventricles whilst

the brain is still *in situ*, or immediately after the skull-cap has been removed, and the membranes examined. In this way all risk of laceration of brain tissue and escape of fluid is done away with.

(*b.*) The other method—one especially adapted for the exact localisation of lesions on the cortex and the secondary changes in the lower parts of the brain in after examination—is that adopted by D. J. Hamilton. The cerebellum, medulla, and pons are removed as in the first method, and then a series of slices is made, each slice being from one-eighth to one-quarter of an inch in thickness, commencing at the tips of the frontal lobes, and passing backwards to the occipital lobes. Each slice is carefully examined, and then, by means of a small parchment or metal label, numbered and put aside for more minute examination.

A modification of this method will also be found useful in certain cases. It consists in making vertical, more or less longitudinal, sections of the brain; the cerebellum, medulla, and upper part of the cord being left *in situ*. Where cortical lesions are followed by secondary degeneration descending to the cord this method is especially useful, as by making the sections in somewhat different planes the lesion may be pretty accurately followed.

11. The directions for taking out the *cord* may be now given, but it is better not to proceed with this until after the thoracic and abdominal viscera have been taken out, when, of course, the body is so much lighter.

The directions given by the German medico-legal authorities (see Dr. T. P. Smith's translation of Virchow) are those which are almost universally followed, and are given in full, as they are in an extremely compact and comprehensible form.

"The vertebral column is to be opened from the posterior aspect. The skin and subcutaneous fat are first to be divided exactly over the spinous processes; the muscles are then to be removed from the sides of these latter, and from the arches of the vertebræ . . .

"Then, by means of a chisel, or a vertebral saw, if at hand, the spinous processes, together with the adjoining portions of the vertebral arches, are to be detached and removed. The dura mater is now exposed, and after its external surface has been examined, it is to be carefully slit open longitudinally, and the presence of any serum or extravasated blood, or other abnormal matters, is to be determined.

"The colour, appearance, and general condition of the posterior portion of the pia mater are next to be noticed, and the resistance to pressure of the spinal cord is to be ascertained by gently passing the finger over it.

"The roots of the nerves are next to be divided on both sides by a longitudinal incision; the lower end of the cord is to be carefully taken out, its anterior connections are next to be gradually separated, and, finally, the superior extremity is to be removed from the occipital foramen.

"In carrying out these directions great care must be taken that the spinal cord be neither pressed nor bent. When removed, the condition of the pia mater on the anterior aspect is first to be examined; then the size and colour (external) of the spinal cord are to be noted; and lastly, numerous transverse incisions are to be made with a very sharp and thin knife, to determine the internal condition of the spinal cord, both of its white strands and of the grey substance. The dura mater is then to be removed from the bodies of the vertebræ, and the dissector is to examine for extravasation of blood, injuries, or alterations in the bones or intervertebral cartilages."

12. To return to the examination of the contents of the thoracic cavity. The various cavities of the *heart* must be opened separately whilst that organ still maintains its relative position to the surrounding structures. It is rotated from left to right, so that the right border of the heart may come to the front, and an incision is made into the right ventricle, commencing at the base, the knife being gradually withdrawn as it nears the apex. In the same plane make an incision into the right auricle from about midway between the two venæ cavæ to very near the base of the heart, then remove, measure, and examine the blood from the right auricle, and examine the tricuspid opening with the fingers, from the auricle, taking care not to

interfere in any way with the segments of the valve. In the same way measure and examine the blood taken from the right ventricle.

To open the left auricle, make an incision, still in the same plane, between the left superior pulmonary vein and a point just on the same side of the coronary vessels (in order that these latter may be left intact).

The left ventricle is also opened by a single cut from "just behind the base" to "just short of the apex," at a distance of about half an inch from the septum. The blood is removed from these two cavities and examined as before, and the size of the mitral orifice determined.

Remove the heart by dividing the aorta and pulmonary artery at some little distance from it; note the size of these vessels, the thickness of their walls, or any abnormal condition, and then carefully clear out all coagula, not only from these vessels, but also from the various orifices, and test the competence or incompetence of the aortic and pulmonary valves by means of a stream of water. To do this with the aortic opening, place the tips of two fingers one in the right auricle and another in the left, and with the tips of one or two fingers of the other hand draw on the pulmonary artery. In this way an equal traction is made at three points, around and in the same plane as the closed valve. Allow water to run in from above, and see whether it runs away or not. If it does, and the water sinks rapidly, cut away the aorta down to within about one inch from the level of the valve, and note at what point the water escapes.

The pulmonary artery is to be tested in the same manner, by fixing the margins of the vessel with the tips of the fingers of both hands, and allowing the water to run in. Take the cone diameters of the various orifices where possible. To make the examination more complete, the cavities of the heart are still further opened up; the right ventricle, by passing a pair of bowel scissors into the opening already made and cutting towards the pulmonary artery, care being taken to avoid injuring the "anterior papillary muscle of the tricuspid valve with its chordæ tendinæ."

To open the left ventricle, cut with the scissors from the apex close to the septum into the aorta, passing "midway between the pulmonary orifice and the left auricle." The auricles are further opened

by incisions, one running from the opening of the superior to that of the inferior vena cava, and that for the left running between the openings of the pulmonary veins. When the cavities are fully opened up the appearances of the tricuspid and mitral valves are to be carefully observed, any thickening, contraction, roughening, new growth, &c. being fully noted and described. Then examine the endocardium, its colour, and the appearance of the muscle beneath, look for clots, especially in the right auricular appendix. Observe the consistence of the muscular tissue by compressing between the fingers, and then slit open the coronary vessels with a pair of probe-pointed scissors or probe-pointed bistoury, look for contractions, atheromatous patches, and so on. Measure the length of the various cavities, the thickness of their walls, and weigh the heart, after which examine the aorta for dilatations or abnormal conditions of the inner coat especially; also examine carefully the pulmonary veins.

13. Remove the *lungs* by cutting through the vessels and bronchi as far from the points of entrance as possible. If there are adhesions which do not at once break down under the fingers, the costal pleura must be dissected away along with the lungs. Examine outer surface of the lungs for exudation, colour, minute hæmorrhages, fibrous nodules, excessive pigmentation along the lines of the interlobular septa, emphysematous bullæ, consolidated patches, or any other abnormal appearances. Then make a long free cut from apex to base, commencing at the outer rounded surface, and passing to the root, so as to bisect the bronchial glands, leaving the two portions attached by the vessels and bronchi forming the root of the lung. Then examine cut surface, note the amount of blood on the surface, and how much may be squeezed out on pressure; note also how much air and serum may be squeezed out, and the colour of the serum. Examine scrapings from the surface, also look for consolidated patches, &c. as seen on surface.

Note the condition of the fibrous septa and of the section of the pleural covering of the lung, the *bronchial glands* (enlargement, caseation, pigmentation), and then with a pair of scissors slit open the branches of the bronchus and pulmonary artery; note the ap-

pearances of the lining membranes of these, and also look for foreign bodies, clots, new growths, or any obstructive mass.

14. It is seldom necessary to examine the parts about the *face* and *ear;* but when this is necessary, the various structures may all be exposed by continuing the vertical incision over the skull, down behind the ears to the neck, throwing the skin forward, so that it may be replaced at the conclusion of the dissection.

15. In the *neck* open the carotid sheath at once, after reflecting the skin, and examine the vessels and the vagus, then the sympathetic ganglia, after which dissect up the larynx, œsophagus, and pharynx *en masse*, and remove along with tongue and soft palate by cutting through the floor of the mouth, and detaching from the base of the skull. Open the tubes and examine for new growths, the condition of the mucous membrane, and then examine in turn the thyroid and salivary glands, the tonsils, and the cervical lymphatic glands.

The examination of the abdominal cavity must now be completed.

16. Take out the *omentum*, noticing any abnormal growths or appearances.

17. Remove the *spleen*, after noting its position and taking measurements whilst the organ is still *in situ*. Weigh the organ and examine the capsule for thickenings or alterations in colour. Make a free incision through the thickest and longest part; note the colour, consistence, amount of blood exuded, the appearances of the trabeculæ, and of the malpighian bodies. Pour a watery solution of iodine over the surface, and examine again. Make other incisions in various directions to complete the examination.

18. Remove and examine each *kidney* separately, first the left, and then the right, taking out at the same time the corresponding suprarenal capsules and the semilunar ganglia, where necessary. To remove the kidney make "a vertical incision through the peritoneum, external to and behind the ascending or descending colon; the

intestine is to be pushed aside, and the kidney detached from its connection." Weigh the organ, and examine the outer surface for evidence of surrounding inflammation, then make an incision from the convex outer border of the organ down to the pelvis, and notice the amount of blood exuding from the cut surface, the colour of the cortex and of the medulla, especially at the bases of the pyramids. Then strip off the capsule, see whether it is thickened, adherent, laminant, &c. Examine the surface, note state of distension of the venæ stellatæ, the colour of the surface, and so on, after which try the consistence of the organ.

The relative proportion of the medulla and cortex are to be observed, the size, patancy, and thickness of the walls of the arteries in the boundary area, the regularity and the size of the malpighian bodies, the appearances of the interlobulary vessels in the cortex and the straight vessels in the pyramids; look for cysts, and then examine the condition of the mucous membrane of the calyces, pelvis, and of the ureter.

Stain a section with watery solution of iodine, and examine especially the malpighian bodies and straight vessels.

19. The *suprarenal capsules* are to be described as to size, colour, consistence, and appearances on section (induration, caseation, waxy appearance, for which apply the watery solution of iodine), and examine along with them the *semilunar ganglia* of the corresponding sides, and any firmness of these ganglia is to be noted, or any signs of inflammatory thickening or pigmentation, where such are present.

20. The *bladder* is next opened *in situ*, and any peculiarity of the mucous membrane, pouches, thickening of the walls, papillomatous growths, deposits of ammoniacal phosphates observed. Remove the contents of the pelvis, and examine the *prostate*, *vesiculæ seminales*, and *urethra* for signs of inflammation, enlargement, or stricture; the *testicle* and *spermatic cord* for caseation, enlargement, or other changes.

21. In the female remove and note the condition of the *vagina*, look for ulceration, new growths, &c. on the os uteri. Examine the *uterus* itself with its appendages, noting carefully the condition of the lining

membrane, the appearances of the vessels, and also any new growths, and their positions; corpora lutea, cicatrices, cysts, or new growths in the ovary.

22. Next cut out the *rectum* after placing on a couple of ligatures; slit it up, and examine its mucous membrane; look for fissures, stricture due to new growths or other causes, for varicose conditions of the veins, &c.

23. At this stage Virchow insists that the *duodenum* and *stomach* should be examined for adhesions or any abnormal appearances, and then opened *in situ* by an incision made with a pair of scissors, running longitudinally along the anterior surface of the duodenum and the greater curvature of the stomach; after this, he says, determine the contents of the duodenum, "above and below the papilla bilaria; then this papilla should be examined, and its contents gently pressed out; then, by pressing on the gall bladder, we should determine the presence or absence of obstacles to the flow of bile; and, lastly, the ductus communis choledochus should be slit up. Then the *vena cava* should be examined, and, all this having been done, the liver should be removed. It is quite useless to pass a probe along the gall duct, for our being able to introduce a probe into the orifice is no evidence whatever that the portio intestinalis was pervious during life."

The *stomach* should be examined at the same time as the duodenum, and any thickening of the pylorus, congestion, or ulceration of the mucous membrane noted.

24. The *liver* may now be removed, weighed, and measured, its shape, its consistence, and resistance noted, the external surface examined for thickenings or any abnormal appearance, then sections made through its substance transversely (from right to left), leaving the sections united by one edge at the under surface of the organ, noting the toughness of the tissue as the knife passes through it, and testing its friability with the fingers, the amount of blood contained, and size of the vessels, the appearance of the capsule on section, the amount of connective tissue, the colour and appearance of each zone

of the lobules (before and after the addition of iodine solution), and the size of the lobules; look for new growths.

25. Then examine the *pancreas*, and take out the semilunar ganglia, if this has not been done when the kidneys were removed; and it is to be remembered that in some cases it is much easier to do it at this stage, when the pancreas has been got out of the way.

26. The *mesentery* and *intestines* are to be examined *in situ*, and any adhesions, new growths, enlarged glands, the condition of the *vessels*, and *lymphatics* observed; then with a sharp knife cut through the attachment of the mesentery close to the intestine, drawing the intestine from the abdominal cavity as this is done; send a stream of water through it to wash out its contents, unless there are special reasons for examining these in the different parts of the intestine; and then slit up the bowel with the bowel scissors, taking care to cut through the walls at the point of attachment to the mesentery. Examine the mucous membrane for thickenings or changes in the various structures, congestion, ulceration, sloughing, perforation, and so on, at the same time examining the mesenteric attachment for tubercle nodules along the lines of the lymphatics, and "in every case of peritoneal inflammation examine carefully the vermiform appendage." Apply iodine to the mucous surface.

27. Lastly, examine the *retro-peritoneal glands*, *thoracic duct*, *receptaculum chyli*, *aorta*, *vena cava*, and the large trunks going into the pelvis; and also, if necessary, examine the sympathetic nervous trunks.

In certain cases other structures have to be examined, or more particular attention has to be paid to certain parts; but the necessity for doing this will be indicated by the clinical history of the case.

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CHAPTER II.

PATHOLOGICAL HISTOLOGY.

28. *Instruments required.*—To the student entering upon this department of pathological investigation, if he has not already made himself, to some extent, master of histological methods, a few words are necessary as to the selection of the apparatus most commonly used in carrying on microscopic work.

The most important part of this apparatus is the microscope, which should never be bought without the assistance of some one well qualified to judge the merits of the instrument.

It may help the student in his selection, however, if a short description of a good compound microscope, such as is suitable for pathological work, be given.

The pedestal must be firm and steady, either a tripod with a good broad base, or a horse-shoe. Fixed into this is a column of sufficient thickness to insure considerable strength, and jointed just below the stage, in order that the whole instrument may be inclined, or bent even to a right angle, if necessary (the tripod should be so based that even in this position the stand remains perfectly steady). The stage should be immoveably fixed into the pillar at a convenient distance from the base, *i.e.*, not so high that the arms may not rest on the table when the fingers of the left hand are moving the slide over its surface. In no case should the transverse diameter of the stage be greater than the length of the ordinary glass slide—three inches. The antero-posterior diameter must not be less than two inches and a half. There should be two brass clips, one on each side of the pillar, fixed into holes in the stage. These are of use in fixing an object in a desired position for examination, and also for controlling the movement of the slide when a high power is used.

Mechanical stages should be avoided, except for use with very high

powers, for two good reasons,—they add enormously to the expense of the instrument, and, for continued work, tire the fingers and hand much more than does the movement of the slide over the simple stage by means of the fingers. In the centre of the stage is an aperture about five-eighths of an inch in diameter. Attached by a screw to the under surface of the stage is a thin plate of metal, in which are cut some five or six holes, varying in size from 1-24th of an inch to three-quarters of an inch in diameter, and so placed, that when the metal disc revolves, the centre of each of these holes is in succession brought under the centre of the large hole in the stage.

In order to bring this metal disc nearer to the upper surface of the stage, the under surface of the stage is bored or recessed. The apertures of the diaphragm are thus brought nearer to the objective. This is especially useful when the higher powers are used with the smaller apertures of the diaphragm, or where it is wished to throw an oblique light up through the specimen under examination. For ordinary work, however, this recessing of the diaphragm is not necessary. At the circumference of the disc, on its under surface, should be small depressions or indentations, into which a spring catch drops, as the centre of each opening comes to the centre of the opening in the stage. The edge of the disc is milled, and its surfaces are blackened. At one side of the stage a slight recess is usually cut out, or the milled edge projects slightly, so that the disc may be readily turned by the tips of the fingers.

Under the stage, and fixed to the pillar above the joint, is a moveable mirror, which can be brought to different distances from the object. For ordinary work a slightly concave surface is used, but for work with an achromatic condenser a flat surface is necessary. This mirror is used for the illumination of objects by transmitted light, or light sent through the object to the eye of the observer; it is therefore especially useful in the examination of transparent objects, which form by far the greater proportion of those objects which come under the notice of the pathologist. In most cases the light is passed directly through; but where the tissues are very delicate and very transparent, it is thrown from beneath obliquely, by which means delicate structure is often brought out much more distinctly.

The part of the microscope above the stage is, however, the more

important. Of this it will be well to describe two forms, and point out the special advantages of each.[1]

The first form has an arm fixed at right angles to the pillar; into this arm is screwed a hollow split tube, about two inches and three-quarters in length; working in this is a telescopic tube, composed of two segments, measuring, when closed, about five inches, and when drawn out to the full extent, seven inches in length. In this case the coarse adjustment is effected by giving a spiral motion to the telescopic tube in the split tube. When the parts are kept *perfectly clean*, this adjustment answers admirably, even with moderately high powers; but when the tubes are allowed to get at all dirty, the force exerted at the end of the lever is apt to render the joints of the microscope somewhat shaky. Otherwise, this is the simplest and cheapest form of coarse adjustment, and, where no nose-piece is used, it is also the best and the most rapid, as the tube can be quickly withdrawn and the lenses changed.

Perfect cleanliness is all that is needed to keep this part of the microscope in good condition; and it is to be remembered that on no account is oil to be used, as its effect is to clog the tubes by accumulating in the slits in the side of the tube.

The fine adjustment is made by means of a milled head placed at the upper end of the pillar. (In the Hartnack microscope this adjustment is of special excellence, and, as a rule, is so fine that very high powers may be used with safety on this stand.) If this is good, the screw should work perfectly steadily, and not "lose time"—*i.e.*, the slightest turn of the screw should alter the focus slightly. The alteration should be smooth and steady, and not in jerks.

The point wherein the second form differs from the first is in the method of making the coarse adjustment, which is effected by means of a rack and pinion movement. This, like the fine adjustment, should be attached to the pedestal, and not to the end of the arm which supports the body of the microscope. The pinion is worked by means of "milled heads," and it should work smoothly and without "any loss of time."

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[1] The first form described is Hartnack's No. III. A.; the second Pillischer's International, with one or other of which the writer usually works.

To the body of the microscope is attached a Bull's-Eye Condenser, consisting of a plano-convex lens, at the end of an arm, in which are three joints. This arm is fixed into a moveable split ring, which fits around the split tube. By means of this arrangement the condenser may be made to focus light directly on to the object under examination, from which it is reflected to the eye. (Care must be taken to have the condenser at right angles to the rays of light.) In some microscopes the condenser is fixed to the stage, but it is in the way there, and is not nearly so convenient as when fixed to the body of the microscope, as mentioned above. This method of illumination is used in the examination of opaque objects, such as sections of waxy liver stained with iodine; but it is not often required in pathological work.

The optical parts of the microscope are naturally the most important—the eye-piece and the objectives. In selecting these, take care to obtain such as will give a magnifying power of about 50 for the low power, and 300 with the higher combination. In the case of the Hartnack, these are approximately given with a No. 3 eye-piece, and objectives Nos. 3 and 7; in the microscopes of English make, ocular No. 3, with one inch and one-sixth or one-seventh of an inch objectives; and in Zeiss's microscopes, ocular No. 3, objectives A. and D. Lower and higher powers may be afterwards obtained for special investigation, but the above lenses will be quite sufficient for ordinary work. In selecting the lenses, note the following points, testing by means (1) of a thin film of blood, and (2) salivary corpuscles. The lens must be perfectly achromatic; the low power should have good definition and a *flat field.* In regard to the low power this is of special importance, as with it the general outlines of the structure are first examined, and it is necessary to have as much of the tissue under observation, in focus at one time, as possible.

Focus the corpuscles in the centre, and then observe whether the corpuscles at the margin of the field are as clearly seen.

The higher power should have *good definition;* the field should also be flat; but this is not of nearly such great importance as the clear definition of delicate structures, such as those seen in a salivary corpuscle.[1]

[1] The demand for good and cheap microscopes has now become so great that a considerable number have lately been offered to the student. From actual ex-

29. The following most useful accessory apparatus may with advantage be procured :—

A double or triple nose-piece properly centred. This will prove a great saving of both time and trouble, especially where the rack and pinion coarse adjustment is used.

An achromatic condenser, or an Abbe's illuminator, is essential when micro-organisms are to be studied.

A microscopic paraffin lamp, with a blue glass chimney, or, what

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perience the author can recommend almost any of the following instruments as being very good and reliable ; but he has no doubt there are others in the market almost, if not quite, as good and cheap. For cheap instruments, those made by Leitz of Wetzler, £3 : 10s. and £5 : 5s., and by J. Parkes & Son of Birmingham, £4 and £6. A little more expensive is Hartnack's No. III. A., with ocular No. 3 and objectives Nos. 3 and 7, which costs about £7 : 10s. (The lower power lens is not always good, and great care should be taken in selecting this objective.) The higher powers are almost invariably good. This has a steady horse-shoe stand, and a very good fine adjustment. Similar microscopes of very great excellence are made by Nachet and Verrick, both of Paris. Carl Zeiss of Jena furnishes a stand V b, with ocular No. 3 and objectives A. and D., for about £9. The lenses made by this maker are uniformly good.

Of the English microscopes, the following may be relied upon as of thoroughly good workmanship, and possessing good optical appliances :—Pillischer's "International," with five-eighths of an inch and one-seventh of an inch objectives, and two eye-pieces, price £7 : 10s. ; a perfect microscope for students, were the tripod slightly firmer and steadier.

R. & J. Beck's "Economic" microscope, with two eye-pieces, objectives one inch and one-eighth of an inch, £8 : 8s., also a first-class instrument, very firm and steady, the only disadvantage being that the coarse adjustment is placed at the end of the arm instead of on the pillar.

Swift & Son's "Improved Wales's American" microscope, with one inch and one-fifth of an inch objectives, and No. 3 eye-piece, £8 ; and C. Coppock's "Combination" microscope, with two eye-pieces and two objectives, one inch and one-sixth of an inch, £8 : 8s., both of which are excellent microscopes for students.

Of the more expensive microscopes one of the best is Zeiss's stand, made in various qualities, of which Nos. IV. to I., ranging in price from £7 : 10s. to £15, may be selected. This is the price of the stand only ; the other appliances, optical and mechanical, may be had up to any sum that the purchaser may feel inclined to expend. For high powers the best objectives are Zeiss's one-eighth inch, or the one-twelfth inch oil immersion by the same maker. Very good and cheap immersion lenses are made by Seibert, successor to Gundlach of Berlin, whose one-sixteenth inch water immersion lenses give exceedingly good definition with even a moderate light. Price, with correction, £3 : 18 : 6 ; without correction for thickness of cover glass, £3 : 3 : 6. Agent in London for both Zeiss and Seibert is C. Baker. The high power lenses made by English makers are excellent in quality, but are generally very high priced.

answers equally well, an argand gas burner fitted with the blue glass chimney. (This combination may be obtained for about 7s. 6d.)

A micrometer eye-piece and a stage micrometer.

A camera lucida, the best and cheapest of which is made by Nachet of Paris.

30. The following apparatus will also be required :—

a. A razor and a couple of scalpels, similar to those already procured. See § 1.

b. Three or four strong needles firmly set in hardwood handles. These should be quite smooth, free from rust, the point perfect, and not hooked or twisted.

c. A couple of pairs of scissors; one pair straight and probe-pointed, the other pair sharp-pointed and curved on the flat. Those used by ophthalmic surgeons answer the purpose admirably.

d. A copper lifter, with a stem about three and three-quarter inches long, and two blades; one about 1 inch × ¾ inch, and the other ⅝ inch × ⅜ inch. The stem should be flat, and the blades continuous with it; very thin, so that they may be bent to form any angle. The edges must be perfectly rounded and smooth.

e. Six or a dozen deep watch glasses.

f. Two or three test glasses and half a dozen test tubes.

g. Half a dozen white earthenware pint basins, and three or four rounded shallow glass trays or capsules. (These latter are especially useful in staining tubercle bacilli, &c. They may be replaced by what are known in the glass trade as clock glasses.)

h. Two or three small glass tube pipettes, for removing fluids of various kinds from the edges of the cover glasses after sections have been mounted.

i. Several goat hair pencils for cementing slides, and a similar number of camel hair pencils for the manipulation of sections, in the process known as pencilling.

j. Six dozen glass slides with ground edges, 3 inches × 1 inch.
Four do. do. do. 3 inches × 1½ inches.

Eight dozen extra thin circular cover glasses, ⅞ inch in diameter.
Five or six dozen do. do. 1¼ inch diameter.
One ounce square cover glasses for use when Canada balsam is the mounting medium.

These, of course, may be replaced from time to time as they are used, but it is well to have at least these numbers, if the student intends to examine the various morbid tissues which come under his notice.

k. Labels for the slides.

l. A small box for carrying six or a dozen slides, and a cabinet to hold the above ten dozen slides, should be obtained, in order that the specimens may be kept clean and well arranged.

N. B.—The slides on which sections are mounted should always be kept flat, and in trays, not boxes.

m. A soft linen cloth. An old pocket handkerchief is, perhaps, the best cloth one can use.

n. A couple of black lead pencils—HB. and HHHH.
Half a dozen lithographic pens.
A small box of moist colours, with brushes.
Some ordinary mounts to be cut into drawing cards.

o. A packet of white filter papers.

p. A freezing microtome (§ 68, p. 49).

31. The following reagents, which should be in one-ounce glass-stoppered bottles. Those marked *R* should have a glass rod nearly as long as the bottle fused into the glass stopper. The end of this rod must be well rounded, *not* pointed. Those marked *W* should be in wide-mouthed glass-stoppered bottles.

REAGENTS IN GENERAL USE.

For staining tissues :—

R. Picro-carmine staining fluid (§ 73, p. 53).
Logwood staining fluid (§ 74, p. 56).
R. Carmine do. do. (§ 75, p. 58).
Methyl aniline violet (§ 76, p. 59).
R. Iodine staining fluid (§ 77, p. 61).
Eosine $\frac{1}{10}$ % solution (§ 79, p. 62).
W. Osmic acid ½ % solution, in bottle covered with brown paper (§ 80, p. 62).

Other reagents :—

Acetic acid, 1 to 4 (§ 93, p. 68).

R. Glacial acetic acid (§ 93, p. 68).
R. Caustic potash 40 °/₀ solution (§ 94, p. 68).
R. Neutral saline solution (¾ % solution of common salt) (§ 34, p. 32).
Bicarbonate of soda, 5 % solution (§ 95, p. 69).
Absolute alcohol (§ 96, p. 69).
Oil of cloves (§ 96, p. 69).

MOUNTING FLUIDS.

R. Farrant's solution (§ 98, p. 71).
R. Glycerine (§ 97, p. 70).
R. Iodine mounting fluid (§ 77, p. 61).
R. Canada balsam, or dammar mounting fluid (§ 100, p. 72).

CEMENTS.

W. French Glue, gold size, or a solution of indiarubber or gelatine (§ 102, p. 73).
W. Zinc white cement, (§ 103, p. 73).
W. Benzole (§ 105, p. 75).
Larger bottles containing—
Methylated spirit.
Distilled water.

SPECIAL REAGENTS.

For staining :—
Aniline blue black (§ 81, p. 63).
Gentian violet (§ 82, p. 63); magenta (§ 83, p. 64); or fuchsin solution, (§ 85, p. 65).
Bismarck brown, chrysoidin or methylene blue solutions (§ 87, p. 65, *et seq*).
Iodine green (§ 90, p. 66).
Other aniline dyes : [1]—
Gold chloride ½ °/₀ solution in distilled water (§ 91, p. 66).
Silver nitrate ½ °/₀solution in distilled water (§ 92, p. 67) (for tumours, &c.).
The bottles in which these two reagents are kept should be carefully covered with brown paper.
Other reagents :—
Nitric acid, 1 in 4 distilled water (§ 66, p. 47).
Turpentine (§ 96, p. 69).
R. Camphor mounting fluid (§ 99, p. 72).

DIRECTIONS FOR WORKING WITH THE MICROSCOPE.

32. Take out the draw-tube and screw on the No. 3 or one-inch objective, use the No. 3 eye-piece and close the telescopic tube, wipe the two ends of the ocular with a piece of soft chamois leather, or a silk

[1] Those who take an interest in special stains are referred to a full description of the various aniline dyes in Dr. Heneage Gibbes's "Practical Histology and Pathology."

handkerchief, using, if the glasses are greasy, a little weak ammonia; then bring the lens nearly down to the level of the stage, and illuminate the field by reflecting the light upwards, by means of the sub-stage mirror, through a large aperture of the diaphragm. The best light to use is that taken from the north, reflected from a bank of white cloud; but, of course, for night-work, lamps as already described must be used. If any specks are visible against the bright field, turn the eye-piece, and if the specks move, they are on the eye-piece and not on the objective. If there is simply blurring or cloudiness of the field, the objective is dirty, and should be cleaned at once. Then, having placed a slide on the stage, gradually draw the tube *upwards*, or work it upwards with the coarse adjustment, at the same time moving the slide over the stage with the left hand, and looking down the tube, until the specimen becomes visible. Then with the fine adjustment bring the object accurately into focus.

By commencing with low powers near the stage (about a quarter of an inch away) there is less danger of bringing a very low power, say a two or four inch objective, down on the slide.

In all cases, the general features of the object should be first carefully studied, as much is to be learned from such a study, which can only be made under the low power.

Place in the centre of the field any part of the object which appears to be specially important, and screw on the high power lens, or turn round the arm of the nose-piece to which the high power lens is screwed. Centre a small aperture of the diaphragm. The lens is to be placed at a distance of a quarter of an inch from the stage, and is gradually brought *down* by means of the coarse adjustment to the point at which the outline of the specimen may be clearly seen (the directions given above as to looking through the microscope whilst the object is being focussed must be borne in mind); then focus more carefully with the fine adjustment. In using the high power, the beginner will from time to time bring the lens down into the Canada balsam, unless very great care be taken to attend to the directions given; and when this occurs, it is well to remember that the Canada balsam may be dissolved off by means of a drop of clove oil, which should, however, be removed at once, or it will loosen the lenses from their setting, where they are cemented with Canada balsam.

In reading the above directions, it will be noticed that nothing has been said about changing the eye-piece. This is intentional, and the student will find that it is better to accustom himself to a single eye-piece, and to alter the magnifying power by means of the objectives, rather than by the eye-piece. With a *perfect* lens, any eye-piece may be used, but where there are the very slightest defects in the lens, these are, of course, magnified by the higher eye-pieces, which magnify only the image given by the objective. The same holds good as regards lengthening the tube. When possible, work with the shorter tube, for, although greater magnifying power is obtained when the tube is drawn out, the definition is not so good, except with first-class lenses, and in a very strong light.

The student should accustom himself to working with the microscope in a vertical position, as the fingers can move the slide much more steadily over a level stage. With the high power, the clips gently pressed down on to the slide will prove of very great service in controlling its movements.

Before setting to work, see that both slides and cover glasses are perfectly clean. The slides, as a rule, are pretty free from grease or hard film when they are supplied, and can be readily cleansed by thoroughly washing them in clean water, and drying them carefully with an old cloth. New cover glasses are generally more or less coated with grease, or with a hard film, which cannot be got rid of by water alone. To cleanse them, put them into a test glass, and cover them with some strong acid (nitric, sulphuric, or acetic), leave them in it for a couple of hours, pour off the acid, and wash well with clean water, then again with methylated spirit, after which they may be dried with an old handkerchief. When once clean, they should always be held by the edges, and never laid down flat, but should be tilted up against the microscope until required. Cover glasses may be cleaned in large quantities, left in water in a covered vessel, and dried as they are required for use.

33. *Method of applying a cover glass.*—Take a cover glass by the edges between the forefinger and thumb of the left hand. Allow the edge to the left to come in contact with the left edge of the drop of mounting fluid. Then with a needle held *under* the right hand,

and under the right edge of the cover, allow it to descend slowly, taking care that it drives the fluid evenly before it and encloses no air bubbles. If this cover is perfectly clean, the operation is readily performed, but if it is at all dirty, a considerable crop of air bubbles is sure to result, though the greatest care be taken. If there are air bubbles in the mounting medium, they should be carefully removed with the point of a needle before the cover glass is applied.

Examination of Fresh Tissues.

34. For the pathologist, much more than the student of histology, it is necessary to examine tissues in a fresh condition. In making such examinations the tissues must be bathed in a medium which will not change either the appearances or the vital properties of their various elements more than is absolutely necessary. Such media are called neutral, normal, or indifferent. Where possible, tissue elements should be examined in the fluid in which they are normally bathed. Pus, blood, &c., always contain sufficient fluid to render the corpuscles easily mounted; and when mounted, the corpuscles remain comparatively unchanged, until the quality of the fluid is altered by evaporation, or until the altered temperature begins to tell upon them. Where larger sections or fragments are to be examined, it is necessary to extemporise a neutral medium in which to bathe the tissue. In the case of gland tissue, nerve fibrils, splenic pulp, and other like delicate and unstable tissues, such a fluid is essential. Any of the following fluids may be used :—

1. Aqueous humour taken from the anterior chamber of the eye of a newly killed ox, by puncturing the cornea with a triangular knife. This of course is available only in small quantities.

2. Serous fluids, such as that taken from the pericardial sac (which is always procurable in the *post mortem* room), or amniotic fluid, which is not so readily obtained.

3. To either of these serous fluids iodine may be added to form *iodised serum*. It is prepared by adding

1 part tincture of iodine to
100 parts of the serous fluid.

To each ounce of the fluid add a couple of drops of carbolic acid,

and filter. This fluid may be kept for some time, but should be prepared fresh whenever opportunity occurs. Its disadvantages are that it alters the tissues slightly, and stains them yellow.

4. *Salt solution.*—Three-quarters per cent. is to all intents and purposes a neutral solution, and is the most convenient of all; in addition to which it alters the tissues but slightly. It is prepared by heating sodium chloride to redness; cooling it over sulphuric acid, and dissolving 7½ parts by weight in 1000 parts by measure of distilled water.

35. Tissues teased out in any of the above fluids, and then mounted in them, retain their normal appearances and structures to a very great extent. To tease out a tissue snip off a small fragment with the curved scissors, put it on a clean glass slide with a small quantity of the neutral fluid; then with one of the needles fix the piece of tissue at one margin, and with the other tear off small fragments; these smaller fragments are fixed with one needle, and torn with the other in just the same manner, until they are small enough to be examined. Put on a cover glass, and then place on the stage of the microscope. In this operation a simple or dissecting microscope will prove of great assistance. This may be easily extemporised out of the bull's-eye condenser by fitting a ring of blackened cardboard into the brass frame, on the plane surface of the condenser. It is used as a simple lens, leaving it attached to the body of the microscope, or fastening it to any upright bar, say of a retort stand. (The perforated cardboard, the student will know, acts as a diaphragm.)

36. The salt solution is also used in the process known as "pencilling." A thin section of the tissue cut fresh and placed on a glass slide is covered with the fluid, and then beaten with a camel hair pencil. In the case of a section of a lymphatic gland, the cells, by this method, are set free from the network of delicate tissue in which they lie, and the different elements may be examined.

A similar result may be more effectually brought about by shaking the section in a test tube containing a quantity of the salt solution.

37. Lastly, thin sections of fresh tissues should always be examined, both unstained and stained.

To make a fresh section of most tissues with an ordinary razor is a matter of very great difficulty, and in its place a Valentine's knife is very frequently used. This instrument is set, to cut sections of a certain thickness, between its two parallel blades; it is then *drawn by a single movement* through the organ of which a section is to be made, then suddenly turned, and a sharp cut made at a considerable angle to the first cut, so as to separate the section from the tissue. The blades are then unscrewed under water (it is best to use the saline solution in which to manipulate the sections so made), and the section transferred to a slide.

38. To transfer to the slide, always have plenty of water in the basin. Take the slide in the left hand, and plunge it into the water in such a position that its under surface forms an angle of about 60° with the table; by moving the slide gently in the water the section is brought from the bottom of the basin (if it has sunk); then, with a needle in the right hand, gently draw one edge of the section on to the slide, fix it there, and withdraw the slide from the water when the part of the section last in the water is floated out on to the slide. The slide is now turned round, and the margin which was first fixed may be floated out in the same way; and underlying or overlapping edges are similarly treated until the section is spread out, perfectly flat, on the glass slip.

Remember in doing this (1) to draw the margin a little beyond the centre of the slide when fixing the first edge, in order that the section may be near the centre; and (2) after fixing the edge with the needle, not to touch the section with the needle again, but to trust entirely to the movement in the water to spread out the crumpled edges. Put on a cover glass (§ 33, p. 30), and examine. A second section is to be stained.

The best stains for these fresh specimens are picro-carmine (§ 73, p. 53); methylaniline violet (§ 76, p. 59); magenta (§ 83, p. 64); methylene blue (§ 89, p. 66); aniline blue black for nerve cells (Bevan Lewis (§ 81, p. 63); and osmic acid (§ 80, p. 62). Mount in glycerine (§ 97, p. 70); Farrant's solution (§ 98, p. 71); or Canada balsam (§ 100, p. 72).

39. A number of fresh sections may be made in a few minutes by means of Cathcart's microtome (§ 68, p. 49). A drop of gum is nearly frozen, then a thin slice of the tissue to be cut is placed on this, a little more gum is painted round the edges, the tissues are frozen just firm enough to cut easily; make sections and mount. This is an extremely satisfactory way of making a microscopic examination in the *post mortem* room, as sections so made are thin enough to be mounted and stained for a more complete examination at a later period, though of course they do not remain unaltered for an indefinite period.

Injection of Tissues.

In particular researches it is often necessary to inject organs or tissues before they are cut up or hardened. In making such injections it is to be remembered that, in the majority of cases, the patient has been dead for twenty-four hours, and that not only have the tissues undergone considerable structural changes during that time, but have become considerably lowered in temperature. For these reasons, a gelatine injection fluid cannot be forced into the smaller ramifications of the blood-vessels, unless certain precautions are observed to prevent solidification of the gelatine fluid taking place. The tissues must be slightly heated throughout up to 100° F., or 38½° C. In some cases such an elevation of temperature might give rise to considerable alterations in the tissues, especially where there is much epithelium, which has already become somewhat changed during the period that has elapsed since death; and here it is necessary to use what may be spoken of as a *cold injection*, or one which is fluid at the ordinary temperature.

40. *Cold Injection Fluid, No.* 1.—*Richardson's Blue.*

Take of

a. Ferric sulphate . . 10 grains.
Distilled water . . 1 ounce—dissolve.

Take of

b. Ferrocyanide of potassium 32 grains.
Distilled water . . 1 ounce—dissolve.

Take of

c. Water	. . . .	2 ounces.
Glycerine	. . . .	1 ounce.
Alcohol	. . .	1 ounce—mix thoroughly.

Add the iron solution gradually to the ferricyanide solution, keeping the mixture well shaken in a bottle. A beautiful greenish blue fluid is the result. Add *c* and shake vigorously. This may be kept always ready for use. Before injecting, however, it is safer to give the bottle another good shaking. This injection is so fine that it may be used for injecting the smallest capillary blood-vessels. For instance, in a leg amputated for a circular ulcer, this injection, forced into the tibial vessels, passes readily into the vascular loops near the surface of the ulcer, giving it a blue colour, where before the injection a raw red appearance was visible.

41. *Cold Injection, No. 2.*

Soluble Prussian blue is also a very convenient form of cold injecting fluid. Buy the Prussian blue ready prepared. Take of

Soluble Prussian blue	. . . .	2 parts.
Distilled water	. . . . .	100 parts.

Dissolve the Prussian blue, and add a few drops of hydrochloric or acetic acid before injecting.

After injection the organ is to be plunged into weak methylated spirit (equal parts of spirit and water), to which a few drops of hydrochloric acid have been added; left there for twenty-four hours, when it may be cut up and the hardening process continued, or it may be hardened from the first in Müller's fluid (§ 53, p. 42), or picric acid (§ 62, p. 46). When sections of these are made, they should again be washed in a weak acid and mounted in camphor mounting fluid (§ 99, p. 72), or in Canada balsam (§ 100, p. 72).

Rutherford mentions two injection masses recommended by Ludwig, which appear to promise well; but the writer has had no experience of their use.

42. The first of them is used for injecting the bile ducts. Asphalte is dissolved in chloroform and filtered. The special advantage of this

fluid is "that chloroform, being an extremely mobile fluid, flows readily along the vessels, and that it readily evaporates and leaves them filled by a solid black mass."

The second, "a solution of alcannin, in turpentine or in chloroform, is used by Ludwig for injecting lymphatics. The solution is of a bright red colour. Both the turpentine and the chloroform flow readily. When the latter is employed the chloroform evaporates, and leaves the alcannin in the vessels."

43. Nitrate of silver cannot as a rule be employed by the pathologist as an injection, as the tissues are dead before he can deal with them, and nitrate of silver does not act at all readily upon dead tissues. In the case of tumours, however, which may be obtained as soon as removed, thin slices of the tissue may be injected by absorption. Thin sections are placed in a half per cent. solution of nitrate of silver (§ 92, p. 67), and left for twelve hours. They are then transferred to a solution of equal parts of methylated spirit and glycerine. After being cut they should be mounted in glycerine.

44. The two following solutions are solid at ordinary temperatures, and can only be used in the case of animals newly killed or where the organs can be warmed to blood-heat.

Carmine Gelatine Injection Mass.

Take of

a. Carmine (pure)	. . .	4 parts by weight.
Liq. ammonia	. . . .	8 parts by measure.
Distilled water	. . . .	100 parts by measure.

Put the carmine in a mortar, and pour on the ammonia, when an almost black paste will be formed if the carmine is pure; pour on the water, and set the solution aside to filter.

b. Take of pure gelatine (Cox and Coignet's) 10 parts by weight, place in a narrow glass jar, and add sufficient distilled water to cover it; allow it to stand until all the water is absorbed, and the gelatine is thoroughly softened.

Warm solution (*a*) in an earthenware jar or basin, placed in a pan of water (kept nearly boiling on a gas jet or near the fire), and add

the gelatine; stir thoroughly, and add a ten per cent. solution of acetic acid, drop by drop, until the alkalinity of the ammonia is neutralised and the fluid even slightly acid.

The point at which this takes place will be recognised by the fact that the pungent odour of the ammonia is gradually lost, and that of acetic acid substituted, and also that a precipitation of the carmine takes place, when the fluid loses its bright carmine transparent colour and turns to a dull brownish red. In order to keep this solution, a small quantity of salicylic acid may be added to the warmed mass. After injection with this fluid, keep the organ for twenty-four hours in equal parts spirit and water, to which some acetic or hydrochloric acid (1 part to 100) has been added. Then continue hardening as directed (§ 52, p. 42), with spirit.

45. *Soluble Prussian Blue and Gelatine Injection Mass.*

a. Take of soluble Prussian blue	.	1 part by weight.
Distilled water	. .	5 parts by measure.

Dissolve thoroughly, add gelatine mass (*b* of carmine gelatine mass), warm in the same manner, and add the salicylic acid. Harden the tissues as directed for the carmine gelatine injection.

In these injections the pigment is soluble in alkaline solutions, but when the acid is added, it is precipitated, and hence cannot diffuse through the tissues, whilst the gelatine still keeps it in a state of exceedingly fine division. This form of injection has this very great advantage over the fluid injections, that it keeps the vessels distended, as the gelatine is rapidly hardened by the action of the alcohol, and is not driven out when the injection tube is withdrawn next day.

Injecting Apparatus.

46. I. Cannulæ of different sizes, which are generally made of brass. The cannula should have a projecting rim near the nozzle, so that, when tied, it cannot slip out of the vessel; there should also be a cross-bar, to which the threads may be fixed after tying round the rim. This, of course, acts as a further preventive to the slipping out of the cannula.

II. (*a.*) A syringe of considerable size; or
(*b.*) A constant pressure apparatus.

III. A piece of brass tubing with a stop-cock.

All the cannulæ are made so that they will fit on to one end of this tube. The other end receives either the nozzle of the syringe or the tube from the constant pressure apparatus.

47. Select the nozzle which appears to be about the size of the vessel to be injected. Make an oblique incision into the vessel, and push in the cannula; pass a piece of strong twine around the vessel and the cannula, and tie firmly, drawing the tube back until the rim comes against the knot; make a second knot, and pass the two ends of the twine around the transverse bars on the tube, and make them fast. Into the open tube drop the injection, drop by drop, until it is full; put in the stop-cock tube with the tap open; fill it in the same way, and turn the tap off. If the syringe is used, it should be of such a size that it will hold from four to six ounces. Fill with the injection fluid, and then turn the nozzle upwards, drive the piston up gently, until all air bubbles are expelled and only the fluid comes. Open the stop-cock and allow the fluid to drop in as before; when the tube is filled, put in the nozzle of the syringe and slowly *rotate* the handle of the piston, and force home, gradually driving the injection into the vessels. *This cannot be done too slowly and steadily.* The syringe may have to be filled several times, and each time the same routine must be gone through in order to keep out air from the vessels.

48. In place of the syringe, the constant pressure apparatus may be used with advantage, as by it the pressure may be graduated to a nicety, and the injection may be made as slowly as is wished. Ludwig's mercury pressure apparatus, or some modification of it, is generally employed; but Stirling's water pressure apparatus is perhaps at once the cheapest, the most readily made, and quite as convenient as any. It is constructed as follows:—Get a large wide-mouthed bottle and a smaller one. Have these well fitted with corks. In the larger cork bore four holes, and in the smaller two. Into two of

the four holes in the larger cork fit two straight tubes, one passing nearly to the bottom of the bottle, the other passing for a distance of half an inch only through the cork. On this latter tube should be a stop-cock, and fitted above it is a mercurial manometer by which the pressure is to be measured. This consists simply of a flattened S-shaped tube turned through a right angle, one bend of which is filled with mercury. Behind this tube is placed an index board marked off in quarter inches. Into the other holes fit a couple of tubes bent at right angles, each passing through the cork and projecting into the bottle for about half an inch, one of them having a stop-cock on the horizontal part of the tube. Into the two holes in the smaller cork are fitted bent tubes, one of which passes to the bottom of the bottle, the other passing in for only half an inch. A tin cylinder holding a couple of pints or more of water is hung over a pulley fixed to the ceiling of the room by means of a cord. It can be raised or lowered at pleasure. An indiarubber tube is carried from the bottom of the tin to the straight tube which passes to the bottom of the larger vessel. From the open bent tube a piece of flexible tubing is carried to the shorter bent tube in the smaller bottle and attached to the longer bent tube in the smaller bottle is a flexible tube with a nozzle which will fit the stop-cock tube fitted into the cannula. The smaller bottle is filled with injection fluid, and both corks are fitted. The stop-cock on the short tube bent at right angles is closed, and the tin vessel is gradually raised; the water runs into the large bottle by the tube passing to the bottom; the air in this large bottle is gradually compressed, and is driven into the smaller bottle, and the increase of pressure above the fluid drives it out of the bottle and into the vessels which are to be injected. As the pressure in the vessels is raised it is indicated by the manometer. This pressure is very readily regulated by merely raising or lowering the tin from which the water gets its "head." The pressure should commence at half an inch of mercury, and be very gradually raised to three or four inches, according to the nature of the organ or tissue which is to be injected.

Where the gelatine injection is used, the organ and the bottle containing the fluid must both be placed in a vessel of water, which should be maintained at a constant temperature of about (never

above) 104° F. (40° C.) for an hour before the injection, and during the time that the injection is running.

N.B.—Always fill the tubes with the injection fluid before attaching to the cannula (the cannula having been already filled), in order that no air may get into the vessels.

Methods of Hardening Tissues.

49. As already mentioned, it is with most tissues an extremely difficult matter to get good sections in a fresh condition. Not only this, but when sections have been obtained, it is found that the structural elements take up so much water that they are not sufficiently well defined, and the examination invariably proves more or less unsatisfactory. To get over the difficulties arising out of these two conditions—*i.e.* to get thin sections and to obviate this absorption of water, and see the tissues in the natural state—it is found necessary to harden them or to "fix the tissue elements as nearly as possible in their normal form and volume."—(Rutherford).

In this fixing, the protoplasm of the cells is toughened and rendered less liable to take up fluids. When working with normal tissues which have been removed perfectly fresh from the body, the greatest care is necessary in the hardening process, and this care is even more necessary in the hardening of pathological specimens which have generally been in the cadaver for at least twenty-four hours, and have therefore undergone considerable change, even in cold weather. For successful pathological investigation so much depends on this preliminary work, that the student is advised to pay attention to even the most minute details in connection with it.

General Directions.

50. *a.* Put the tissues away *at once* in the hardening fluid.

b. Cut up the organ with a *sharp knife* or razor (making clean cuts, not dragging or tearing the tissue) into blocks about one inch square and half an inch thick, or cubes, each side of which measures about three quarters of an inch.

c. Put a bit of rag or some cotton wool, saturated with the hardening fluid, in the bottom of a wide-mouthed jar, then put in four or five of the blocks of tissue; if more than these are required, put in a

second layer of rag or wadding, a second layer of tissue, and so on, but the proportion of tissue to fluid should never be greater than 1 to 20. Fill the jar with fluid, label carefully with the name, age, and sex of the patient, the organ, the supposed morbid condition, and the date and time of the commencement of the hardening process, and its nature. Put it away in a cool dark place; an underground cellar is as good a place as can be used.

d. At the end of twenty-four hours pour out the hardening fluid, carefully wash out the jar and rinse the tissue thoroughly with water to get clear of any blood or other deposit which may have settled, and which would, if left, seriously interfere with the hardening process. As a general rule fluids have again to be changed at the end of the third day, and then weekly for two or three weeks.

e. The tissue should be carefully examined each time the fluid is changed, and its consistency ascertained. When the hardening has gone on satisfactorily the tissues are tough and firm. They should never be allowed to become brittle, which they do if the hardening process is carried on too far or imperfectly.

f. After being hardened slowly, the tissues are removed from the fluid generally about the end of the second to the eighth week, according to the fluid used, and if not hardened in spirit they are washed for several hours in water until no yellow coloration is given to it; after which they are transferred to a mixture of equal parts of methylated spirit and water for a couple of days, and then to methylated spirit, in which they are left until required. The spirit may become cloudy, in which case it must be changed, and again as often as the cloudiness appears.

g. As to the fluid to be used in individual cases, it is an extremely difficult matter to give definite instructions, but the following general rules will assist materially in determining what should be the nature of the fluid used:—

(*a*) Where a tissue is hard and firm, and not likely to shrivel on the abstraction of water, and where, too, it is not thought necessary to keep the blood in the organ, methylated spirit may be used.

(*b.*) Where there is much blood in the tissue to be hardened, or where it is very soft or œdematous, use Müller's fluid.

(*c.*) For the very delicate structures of small objects use osmic acid.

(*d.*) If bacilli or bacteria are suspected, always use absolute alcohol.

Hardening Fluids.

51. *Absolute alcohol* hardens tissues very rapidly. For the intestines, stomach, and pancreas, dip the pieces into methylated spirit, and then place in a bottle in sufficient absolute alcohol to cover them; at the end of twenty-four hours wash again in methylated spirit, and then pour over them about twenty times their volume of the alcohol. For tubercle of organs, anthrax specimens, &c., plunge at once into a large quantity of absolute alcohol, and leave them till thoroughly hardened.

52. *Methylated spirit* is used principally to complete the hardening process, but it may also be used as above for very firm tissues, especially where there is a large proportion of epithelium in a fresh condition. If used alone, as for waxy liver, it is changed at the end of twenty-four hours, and again at the end of a week. Tissues hardened in this way are ready for examination at the end of a fortnight. With most tissues hardened in this spirit, it is well to put them away in equal parts of spirit and water, and only to put them into strong spirit at the end of twenty-four hours; or at this stage to add weak spirit again, and at the end of forty-eight hours change into strong spirit. It is here specially necessary to wash away all the precipitated blood, which will be found to have accumulated in considerable quantities. Change the spirit at the end of the first week, and cut the tissue at the end of a fortnight. In combination with other fluids, methylated spirit is of very great value.

Chromic acid, alone or in the form of some salt, is of all reagents most frequently used. Of the combinations into which it enters—

53. *Müller's fluid* is the most useful, especially in the preparation of delicate tissues, where it fixes the protoplasm of the cells rather than

hardens them, and in this way causes but little shrinking of the tissues, so that for congested organs or mucoid tissues it is invaluable. To prepare it, take of

Potassium bichromate	2¼ parts.
Sodium sulphate	1 part.
Water	100 parts.

Care is to be taken to put in only one volume of tissue to twenty of fluid, as with all other methods. Change the fluid at the end of the first, third, and seventh days, and then at the end of each week till the end of the fifth; transfer to water for several hours after the tissue has been in the fluid for six or eight weeks, and then again to dilute methylated spirit; leave in this for from twenty-four to forty-eight hours, and then preserve in strong methylated spirit. The great advantage of Müller's fluid is, that there is no great danger of over-hardening, and although the process takes a considerable time, the results are almost invariably satisfactory. It appears that the sulphate of sodium can penetrate almost any tissues, and where it once gets in, the bichromate salt can follow. Consequently, it is not so essential that the pieces should be small. This fluid is therefore used where it would be inconvenient to cut up the tissue into small cubes. Commence the hardening process as soon as the structures are taken from the body, and carry on, for the first few days at any rate, in a cool dark place.

54. *Müller's fluid and spirit* for hardening nerve tissues, brain, spinal cord, retina, intestinal muscle and glands, is perhaps one of the best, and is composed of

Müller's fluid	3 parts.
Methylated spirit	1 part.

Cool thoroughly before using.

In the case of the brain, the vessels may be injected daily with this fluid before it is cut up. It is kept for four or five days in a jar of the same fluid, which has to be changed daily, and then it may be cut up as described (§ 10, p. 13.) After being in this fluid for three or four weeks, the hardening process is to be continued with bichromate of ammonia for a fortnight. For hardening other tissues follow the directions given for hardening with Müller's fluid.

55. *Bichromate of potash* (saturated solution) may also be used for hardening pieces of tissue of considerable size, especially of the brain. It must be used in large quantities, to which carbolic acid is added (one or two grains to the ounce), and the fluid is not changed, but kept saturated by the addition, from time to time, of crystals of the bichromate salt. It hardens slowly—in six or eight weeks. Keep in a cool dark place.

56. *Bichromate of ammonia*, as a two per cent. solution, may be used either to harden or complete the hardening of the nerve centres especially, but it may be used for almost any tissue. Use at least twenty volumes of fluid to one of tissue, change at the end of the first, third, and seventh days, and at the end of the second, third, and fifth weeks.

57. Where it is wished to harden tissues more rapidly, a solution of *chromic acid* may be used. It should not be stronger than one-sixth per cent. solution, or the outside only of the cube is hardened, and that is rendered brittle. Where this or any of the following chromic acid compounds are employed, it is to be remembered that the pieces of tissue must be very small indeed (except in the case of the lung); they should never be more than half an inch in any diameter. Use twenty volumes of the fluid to one of the tissue. Change at the end of twenty-four hours, again on the second and third days, and then every third day until the tissue is hard and tough. A careful examination should be made about the eighth day to see that the hardening is progressing properly; for if the tissues are left in the chromic acid mixture too long they may become exceedingly brittle. Wash well, allowing a stream of water to run over the material for several hours; then add equal parts of methylated spirit and water, leave for twenty-four hours, and replace by pure methylated spirit.

58. In place of pure chromic acid a mixture of *chromic acid and spirit* is frequently used:—

Chromic acid, one-sixth to one-third per cent. solution, 2 parts.
Methylated spirit, ... 1 part.

Change the fluid three times—once a day for three days; after this

gradually increase the proportion of spirit in the fluid, until at last only methylated spirit is used. Such a method answers admirably for hardening the lung, which process is completed in about a fortnight, if the fluid is changed every three days after the alteration in the proportion of the fluids has commenced.

59. *Ammonium chromate.*—Five per cent. solution, filtered, and kept in a stoppered bottle, hardens small pieces of tissue, or pieces of the mesentery in twenty-four to forty-eight hours, and is especially useful in studying cell structure. In employing this mixture, cut the tissues into very small pieces, not more than about one-sixth to one-quarter inch in diameter; place in about ten to fifteen volumes of the fluid; leave until hardened (never for longer than forty-eight hours); wash thoroughly in water; and cut at once, or transfer to weak and then to strong spirit, which will preserve the tissue until required.

None of the above hardening media give a permanent colour to the tissues; but the two following not only harden, but also stain the tissues.

60. *Osmic acid.*—One-sixth to one-half per cent. (See § 80, p. 62.)

61. *Picric acid.*—To make which, fill a bottle with distilled water, add excess of crystals of the acid, and simply fill up with water as the fluid is used, keeping the crystals in the bottle to maintain saturation. Tissues should never be allowed to remain in this for more than forty-eight hours; afterwards treat as for chromate of ammonia. The great advantage of this method of hardening is its rapidity, and the fact that tissues thus hardened are stained most beautifully with picro-carmine. It is especially useful for tumours and epithelial or epidermic structures generally, for mesentery, and for small pieces of gland.

Kleinenberg's picric acid, for hardening soft sarcomata, myxomatous tissues, and embryonic tissues, is generally made as follows:—

Saturated watery solution of picric acid, .	100 parts.
Strong sulphuric acid, ...	2 parts.

Filter to remove a yellow precipitate which is formed, and add

Distilled water, ...	300 parts.

It will harden the above tissues in from three to twelve hours.

Decalcifying Solutions,

For removing lime salts from bone and teeth, which at the same time harden the organic matter.

62. *Picric acid saturated solution*, made as above.

It takes some time (two or three weeks) to decalcify bone; it is especially useful for softening young bones. Use a large quantity of the fluid, and add crystals from time to time; it is not necessary to change at all until the bone is ready for cutting; when the bone is ready, wash out the picric acid by soaking in water, and transfer first to weak and then to strong spirit to preserve the specimen.

63. *Chromic and nitric acid fluid* is made as follows:—Take of

Chromic acid . . .	1 part.
Distilled water . . .	200 parts.

Dissolve, and add

Strong nitric acid . .	2 parts.

Put small pieces of bone into twenty times their volume of this fluid; change every third day until the end of the second week; wash well in water for twenty-four hours, and transfer first to weak and then to strong spirit (§ 57, p. 44).

The best results are obtained by this method; the organic parts of the bone are hardened, whilst the nitric acid removes very thoroughly all the calcareous materials.

Simple Decalcifying Solutions.

64. *Hydrochloric acid*, ten per cent. solution. This removes the calcareous matter very thoroughly, but, at the same time, it causes the fibrous tissue to swell up. It is useful, however, for softening injected bone. When it is wished to prevent the swelling of the softened fibrous tissue Ebner's solution is used.

65. *Ebner's solution.*—To prepare this take of

Common salt	10 parts.
Water	100 parts.
Hydrochloric acid	1 part.

Use two or three hundred volumes of this to each volume of bone, and add sufficient acid day by day to thoroughly decalcify the bone. When this is brought about, the bone may be bent like a piece of indiarubber. It should then be thoroughly washed in water for a few hours, and transferred to a ten per cent. salt solution until all acid reaction disappears (change the salt solution daily). Mount the sections in the ten per cent. salt solution.

Fluids used for softening other Tissues, or dissolving out certain substances, so as to set free the individual elements.

66. There are numerous substances recommended in the physiological text-books, but the following will be found to be the most useful for dissociating pathological tissues :—

Iodised serum (§ 34, p. 31) dissolves the intercellular cement substance in about thirty-six hours. It is also useful for macerating white nerve fibres.

Common salt, ten per cent. solution, may be used to soften the cement substance of white fibrous tissue. It is useful in the study of fibromata, osteo-sarcomata, and similar growths.

Caustic potash, forty per cent. solution, is useful for isolating muscle cells, as in the case of myoma uteri. This is very rapidly accomplished, seldom taking longer than from twenty minutes to an hour. Tease out, stain with picro-carmine (§ 73, p. 53), and mount in glycerine (§ 97, p. 70). If time is available, and a permanent preparation of the muscle cells from such growths is required, use—

Nitric acid, twenty per cent. solution.—Place small fragments of the muscular tissue in this fluid, and leave for twenty-four hours. They are then well washed in water, teased out, stained, and mounted in glycerine. By this method the connective tissue is softened, and the muscular fibre is hardened. A similar fluid for isolating nerve structures is often useful :—

Glycerine	1 part.
Water	3 parts.
Strong nitric acid	1 part.

Mix thoroughly. Place small fragments of the tissue in this fluid, leave for three or four days, and then wash well with distilled water.

These methods of softening tissues are naturally to be associated with teasing out tissues, already described (§ 35, p. 32), and are of special importance in the study of the elements of which morbid growths are composed. In addition to the above methods, physiologists use various methods of artificial digestion, which may yet prove useful in pathological research. For these the student is referred to hand-books of physiology and histology.

Methods of Cutting Sections.

67. Freezing microtomes are now to be obtained so cheaply, that it is unnecessary for the busy student to waste time in learning to cut sections by hand. Nor is it desirable here to enter into a description of a process which involves the consumption of much valuable time before the student can attain even moderate proficiency, when, by means of the freezing microtome, results almost perfect, with even the most delicate structures, may be attained with a couple of days' practice. Various modifications of the freezing method have been suggested from time to time. Of these D. J. Hamilton's method is undoubtedly the most perfect in many ways, especially as it involves no danger of overfreezing. To prepare the tissues for section cutting, proceed as follows :—

Remove the hardening fluid from the tissue, especially if spirit has been used, by a prolonged immersion (say for twenty-four hours) in water, which should be constantly changed by allowing a very small stream from the tap to fall into the vessel. Then transfer to a mixture of gum, B. P. strength, five parts, syrup three parts; for retina, brain, or cord, gum five parts, syrup four parts.[1] Allow the tissue to remain in this mixture for from twenty-four to forty-eight hours, or even longer. When it is left in longer than this, a few drops of carbolic acid should be added to each ounce of the fluid, to prevent the formation of fungi. If this be attended to, the tissue may be left

[1] The syrup is made by boiling one part of crystallized sugar in one part of distilled water until the whole of the sugar is dissolved.

soaking in the solution for an indefinite length of time, and at the end will "cut" perfectly, if it has been properly hardened in the first instance. The microtome is cooled down to such a point that a drop of gum (B. P. solution) placed on the die or disc (to be afterwards described) is frozen. The tissue which has been soaking in the gum and syrup is taken out with a pair of forceps, gently dried in the folds of a soft cloth, put to soak for a few minutes in gum, and then adjusted as required on the surface of the frozen gum; more gum is painted on the disc around the piece of tissue, to keep it in position, and to form with it a solid firm mass, which may be cut in a single section. The mass is frozen just so hard that it will cut like a piece of cheese; when softer than this, it is not sufficiently frozen, and when harder, it is very difficult to cut, especially if the sections are of considerable size.

The Freezing Microtome.

68. There are several very convenient forms, but it will be necessary here to describe three only—two for freezing with ice, and one for ether freezing. For an instrument which is ready for use at a moment's notice, Cathcart's ether microtome appears to be undoubtedly the best, and from the student's point of view, it has several very great advantages. It is portable, very clean to work with, its initial cost is moderate, and it can be very inexpensively worked. It is based on a hardwood frame, which may by means of a clamp be firmly fixed to the table; screwed to this is a hollow cylinder, on the top of which is a roughened zinc plate. On each side of the zinc plate is a strip of glass cemented to the wooden frame. By means of a fine-threaded screw, the hollow cylinder, and with it the zinc plate, is raised or lowered at will, through a distance of a quarter of an inch. A double tube is introduced into the hollow cylinder, through one part of which air is driven by a small indiarubber ball arrangement. This stream of air rushing over the mouth of the other part of the tube (which is connected with a bottle of ether) creates a vacuum, and ether is drawn through a small hole; the stream of air completely vaporizes the ether in the chamber under the zinc plate, the temperature of the plate is very rapidly reduced, and the piece of tissue, fixed on with gum (§ 67), is frozen.

The best instrument to use for making the sections is the blade of a carpenter's smoothing plane, used either with or without a wooden handle. It works on the two glass runners, so that the centre of the blade comes in contact with nothing but the material to be cut, and consequently it remains sharp much longer than where there is simply a hole in the glass plate, as in some of the other microtomes. The elevating screw is worked with the left hand, and the knife with the right. In very hot weather it may be found necessary to stop now and again to keep the tissue hard, or the freezing apparatus may be handed over to an assistant. The screw which raises the disc should be kept moistened with glycerine, not oil, as the latter freezes too readily.[1]

This instrument is invaluable for the *post mortem* room (especially in summer when ice is scarce), and for cutting hardened specimens it is also extremely useful and economical, as pieces of tissue up to a quarter of an inch thick may be cut with the expenditure of little more than a halfpenny worth of ether.

Ice-Freezing Microtomes.

69. Of these, Rutherford's and Williams's are undoubtedly the best. Rutherford's consists of a freezing-box, covered with gutta-percha, which acts as a non-conductor, with a drain at one corner. The freezing-box surrounds a well, in which is placed a hollow cylinder with a thread on the inner wall, and covered in at the top with a grooved disc. Into the hollow cylinder a fixed screw is so fitted that when it is turned the cylinder rises or falls. Above the well, and partly covering it in, is a metal plate covered with glass, on which the knife works. Before commencing to work with this instrument, have at hand some finely powdered ice or snow, some coarse salt, a little glycerine, some thick gum, a piece of clean cork (a fresh cut surface of a pickle bottle cork answers very well), and a clean cloth. Screw the cylinder up to the surface, take it out and smear a very small quantity of glycerine over the screw in the well on the inner and outer surfaces of the cylinder, and on the inner surface of the well; then screw down the cylinder until

[1] This instrument, with all necessary apparatus (except the knife), may be obtained from A. Fraser, 7 Lothian Street, Edinburgh, price 15s. The planing-iron may be obtained for about a shilling from any tool warehouse.

there is sufficient depth to take in the tissue. Fill the freezing-box with alternate layers of the powdered ice and salt, taking care to keep the drain freely open, and keep well mixed until the appearance of hoar frost is seen on the outer surface of the gutta-percha. Pour on to the notched die at the bottom of the well a drop of gum solution, made by adding one part of gum to two parts of water. Remove the section from the gum and syrup solution, and place it on the drop of gum as soon as the first sign of freezing of the gum makes its appearance at the margin. Hold it in the position required until it is firmly fixed. Then pour into the well sufficient gum to cover the specimen completely; put on the cork, and weight down until the freezing process is completed. The best knife to use with this microtome is undoubtedly the planing-iron, already recommended for the Cathcart microtome. Remove the sections from the knife with a camel's hair pencil, and treat as below (§ 71, p. 52).

70. Williams's ice-freezing microtome is also an excellent instrument, By the aid of this sections may be cut very rapidly with a little practice. The freezing part consists of a round wooden box with a drain pipe. The inner surface of the box is pitched or tarred to make it water-tight. In the centre of this is a stout brass pillar, screwed firmly down. To the upper surface of the pillar dies of various sizes may be screwed in, for the reception of larger or smaller specimens. Covering the box is a lid, on which is a plate of glass. In the centre of this lid is a round opening, through which the die may be adjusted to the level of the upper surface of the glass. The cutting part of the apparatus consists of a razor, fitted into a triangular frame supported on three legs; each leg is a screw, one in front and two behind, and by raising or depressing these screws the distance of the triangle from the plate may be altered at will, and with the triangle, the razor. The edge of the razor is thus let down when the triangle is depressed in front, by simply turning the front screw out of the frame. (Thus, instead of bringing the tissue up to the razor, the edge of the razor is brought down to the tissue.) Fill the ice-box with salt and ice, layer upon layer, until the box is full; in summer this must be carefully attended to, but in winter the tissue will be frozen sufficiently hard if the box is but half filled. Fasten on the lid, screw in

one of the dies, and fix on to it the tissue to be cut, in the same manner as in the Cathcart microtome. By means of the three screws bring the razor down to the level of the tissue, taking care to have all three legs equal in length. Grasp the tripod in the two hands, and with the forefinger give the large head of the screw at the apex of the triangle a turn through a very small angle, and push the frame, and with it the knife, obliquely forwards, keeping the three ivory tipped legs resting firmly on the glass plate. A thin section will be cut off, the thickness of which is graduated by the angle through which the front screw is turned. The thawing gum is quite sufficient to keep the knife moistened.

71. If the tissue is a very delicate one, the sections, however made, must be transferred separately to a glass slide by means of a camel's hair pencil, and must then be floated out and washed in a mixture of methylated spirit, one part to two parts of water. But with ordinary tissues the sections are transferred to a basin of water, where they may be left from two to six hours (according to the temperature), after which the water should be changed and the sections left for a quarter of an hour, in order that the syrup and gum may be thoroughly washed out. If it is then found that air bubbles are entangled in the sections, they should be well washed in methylated spirit and afterwards in water. They may then be stained and examined, or, if this should not be convenient, they may be kept for a considerable length of time in a mixture of equal parts of methylated spirit and glycerine, or in preservative fluid, which is made as follows :—Take of

Glycerine	15 parts.
Water	15 parts.
Carbolic acid 1-20	1 part.

Or pure methylated spirit may be used to preserve sections, especially if they are unstained.

Methods of Staining Sections.

72. In all cases sections should be examined first unstained ; but even when this is done there is still much to be learned from a study of

the tissues after they have been acted upon by various reagents. Whatever may be the nature of the reagents used, they have all this peculiarity—that by their aid special structures are brought out more prominently, or one tissue is differentiated in appearance from the other tissue in which it lies. Thus it has been found that certain vital parts of cells are more deeply stained by most staining reagents (carmine, &c.) than are the surrounding parts; or, again, a few reagents (picric acid) have a special affinity for the formed material of the cell, or the cement substance may be specially picked out, as by nitrate of silver; certain parts may become "cleared up," and so leave other structures to be seen more easily and distinctly.

In the following directions given for staining tissues special prominence will be accorded to such methods as are found to be most useful to the pathological histologist, which methods, by no means complicated, usually give most satisfactory results.

73. *Picro-Carmine.*—By far the most useful staining reagent at present in the hands of the histologist is Ranvier's picro-carmine staining fluid, or picro-carminate of ammonia. When the fluid is properly prepared and the staining process is well carried out, the most brilliant double-staining effects are obtained.

It is prepared as follows:—Take of

Pure carmine	1 part.
Strong ammonia	3 parts.
Distilled water	3 parts.

Dissolve the carmine in a test tube with the ammonia and water. To this add two hundred parts of a cold, saturated, and filtered solution of picric acid, and mix thoroughly. Place the fluid in a basin and cover with a clock glass (with the convex surface upwards to keep out dust), and allow it to evaporate in *strong sunlight*, testing it every few days by staining a section of skin (see below), until the nuclei and fibrous tissue are stained distinctly pink, and the epithelial cells, especially those of the horny layer, are stained yellow. The best double-staining is usually given before the fluid has evaporated down to half its bulk, and at this stage it is sometimes found that crystals of picric acid are deposited in the tissues. To obviate this, it is necessary to add ten or twenty parts of distilled water. To pre-

vent the growth of fungi add two drops of 1-20 carbolic acid solution to each ounce of the fluid; filter, and keep in a glass-stoppered bottle.

To stain a section, lay it out flat on the glass slip (§ 38, p. 33), drain off the superfluous water, and run several drops of the staining fluid (not diluted) over it; allow it to stand for from three to five minutes exposed to sunlight, covered with a watch-glass to keep off the dust. (In winter it is well to warm gently over a spirit lamp the slide on which the section is being stained, as slight heat causes the tissues to stain both more rapidly and more brilliantly.)

Do not wash the section, but simply run off the superfluous fluid by tilting the slide and then wiping round the section with the

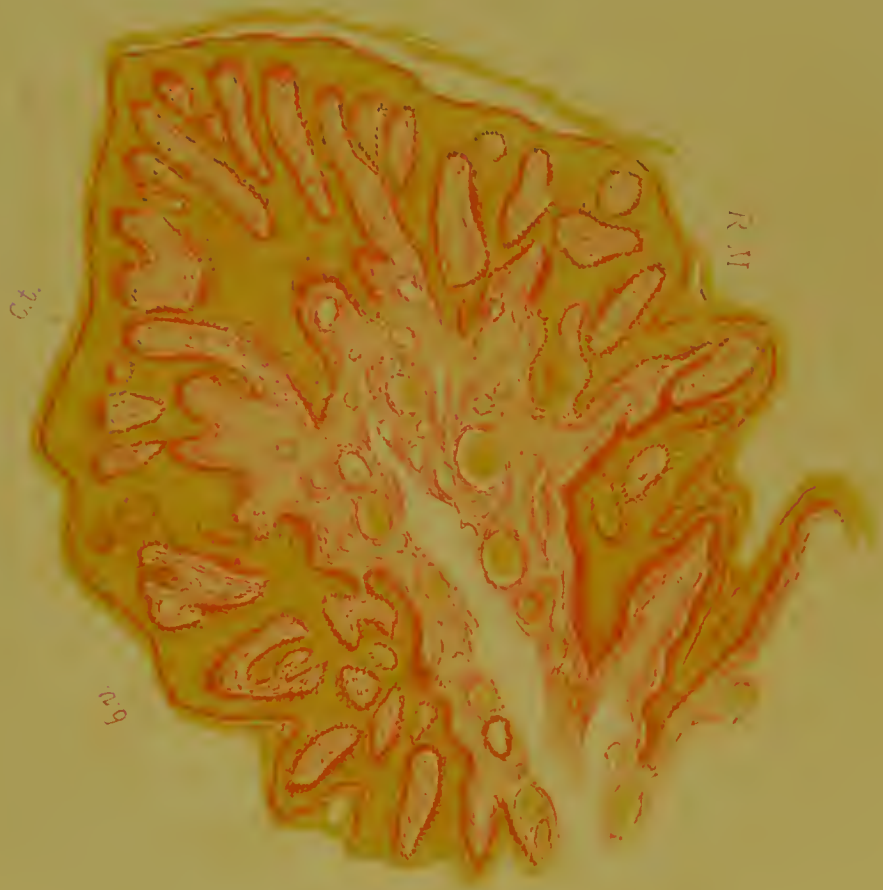


FIG. 1.—Section of papilloma stained with picro-carmine (× 50).
c. Horny layer stained yellow.
R.M. Rete Malpighii, various shades of yellow; nuclei crimson.
C.t. Connective tissue, pink.
b.v. Blood-vessels, in which blood is green.

thumb, or a very soft clean cloth; but be careful not to remove the whole of the staining fluid, as any slight excess is gradually taken up by the tissues after the section has been mounted in either Farrant's solution (§ 98, p. 71), or glycerine (§ 97, p. 70), to which from one to five per cent. of formic acid has been added. (Never mount a picro-carmine stained specimen in Canada balsam or dammar mounting fluid, or the operator will be disappointed with the results.) The full effects of the stain are not seen at

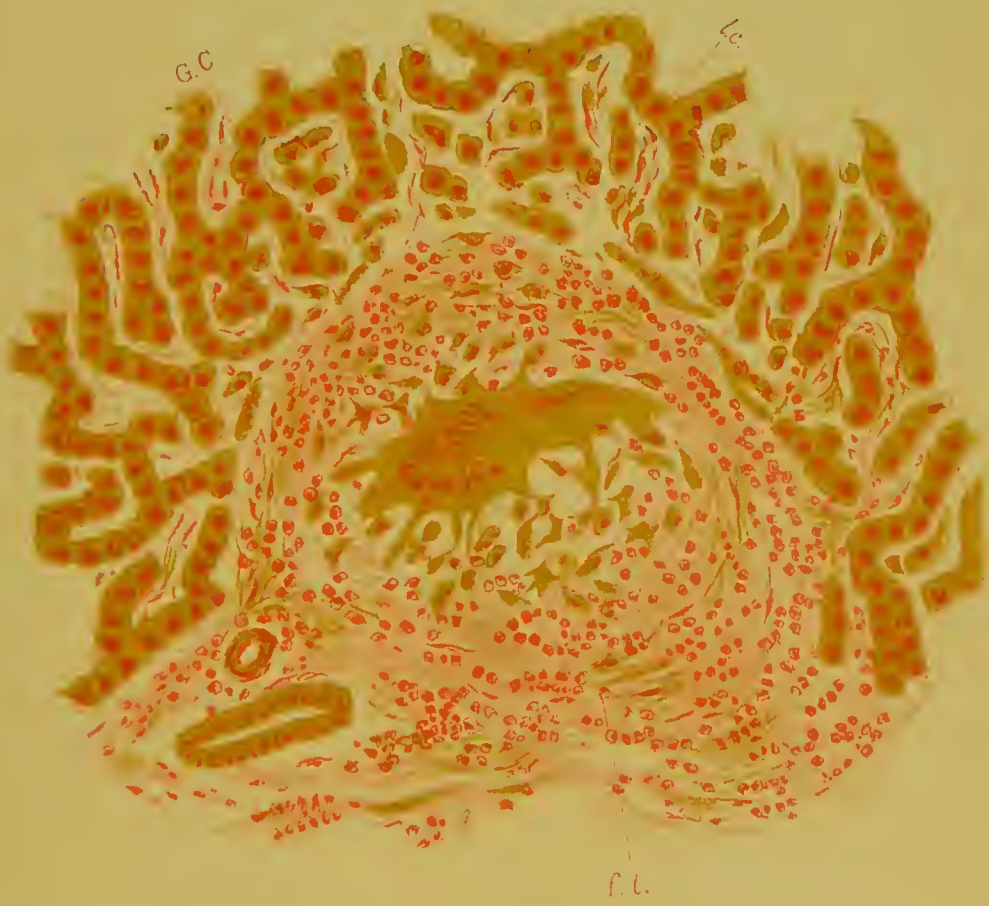


FIG. 2.—Section of tubercle follicle of the liver, stained with picro-carmine (× 300).

l.c. Liver cells stained yellowish brown; nuclei crimson.
G.C. Giant cell stained yellow in centre; nuclei crimson.
f.t. Fibrous tissue stained pink; nuclei crimson.

first, but after the section has been mounted for two or three days, especially if a small quantity of the staining fluid has been left on the section, a beautiful selective double-staining is found. Tissues of high vitality and fibrous tissue are stained a brilliant crimson or pink, whilst the formed material of epithelial cells, elastic tissue, and dead material are stained yellow. Thus, in a section of the skin, the horny layer, the stratum Malpighii, hairs and muscles, are stained various shades of yellow, whilst the nuclei of the cells in the deeper layers of the epidermis are stained crimson, as also is the tissue of the cutis vera (Fig. 1). In a section of a scirrhus cancer the stroma is stained a delicate pink, the indifferent tissue, which is made up of rapidly proliferating connective tissue corpuscles and leucocytes, takes on a rich crimson colour, whilst the cancer cells are stained yellow, the nuclei appearing of the same tint as the cells of the indifferent tissue.

In a section through a tubercle follicle the double-staining also comes out well. The centre of the giant cell is of a canary yellow colour; surrounding this is generally a zone of nuclei, stained a brilliant orange red, outside which is the reticulum with the endothelioid cells stained crimson (Fig. 2); and then at the periphery is the condensed fibrous-looking capsule stained pink, and the small round cell formation, stained much as in the indifferent tissue of the scirrhus cancer. Where caseation has commenced in the centre of the tubercle follicle, there is a yellow granular-looking mass of dead material (stained by the picric acid).

74. *Logwood Staining Fluid.*—This is especially useful for bringing out the nuclear structures in the tissues, and it has the special advantage that it also stains slightly the protoplasm of cells and the fibrilla elements in the tissues (Fig. 3). It may be made in either of the following ways :—Take of

(*a*)	Extract of hæmatoxylin . . .	1 drachm.
	Alum	20 grains.
	Glycerine	10 ounces.
	Water	20 ounces.

Mix the logwood, alum, and water, and allow to stand for four days, shaking them well three or four times a day. Add the glycerine and

boil down to twenty-five ounces, throwing in two or three grains of alum, whereupon the colour becomes much more brilliant. Add two drachms of carbolic acid in order to preserve the fluid.

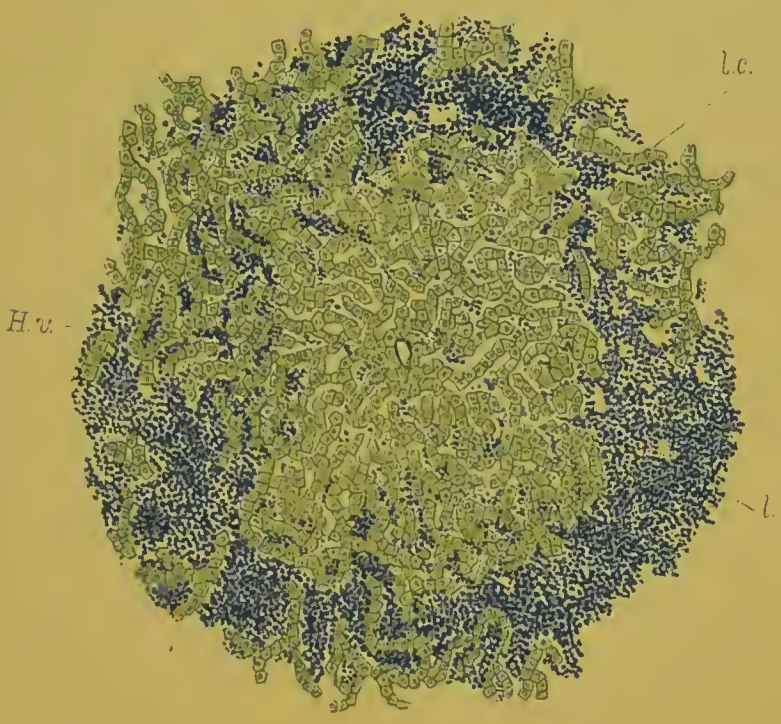


FIG. 3.—Section of leucocythemic liver stained with logwood (× 70).
H.v. Central or Hepatic vein.
l. Leucocytes, especially numerous at the periphery of the lobule.
l.c. Rows of liver cells between capillary vessels.

(*b*) Cook's method of making logwood solution, which is also an exceedingly good one. Take of

Extract of hæmatoxylin	6 parts.
Alum	6 parts.
Cupric sulphate	1 part.
Distilled water	40 parts.

(Great care must be taken that none of the ingredients contain any trace of iron.) Grind the alum and cupric sulphate in a mortar, and add the extract of hæmatoxylin, mix thoroughly, and add sufficient water to form a thin paste. Leave this for one or two days, add the remainder of the water, and filter. Add a crystal of thymol,

dissolved in alcohol, to prevent the formation of fungi. Sections hardened in alcohol take up this staining very readily; but when chromic acid, picric acid, or bichromate solution has been used, it is necessary to wash out the whole of the salt, before attempting to stain with this reagent.

To stain sections, filter about half a drachm of (*a*) or ten drops of (*b*) [to (*b*) add half a drachm of distilled water] into a watch-glass; allow the sections to remain for about three or four minutes in (*a*), or half a minute in (*b*); wash well in water, and mount in Canada balsam (§ 100, p. 72).

Note.—Never put more than two or three sections at a time into the watch-glass, or they cling together, and are unequally stained. Should the staining be too intense, place the sections in a watch-glass, pour a few drops of strong acetic acid over them, then wash and mount.

75. *Carmine staining fluid* is especially useful for sections of the central nervous system, and for tissues in which are considerable quantities of fibrous tissue. As a staining reagent for most tissues, it has been superseded by logwood and picro-carmine. To prepare it, take of

Pure carmine	1 drachm.
Strong ammonia	1 drachm.
Water	6 ounces.

Triturate the carmine in a mortar, add sufficient water to form a paste, and then add the ammonia, when the paste will at once turn from a bright red to an almost black colour if the carmine is pure. Add the rest of the water and keep the solution in a glass-stoppered bottle, with a piece of camphor suspended in the fluid.

After carefully washing out picric acid or any of the chromates, a section may be stained rapidly by laying it out on the glass slide, (§ 38, p. 33), and running a drop or two of the solution over it; allow it to stand for about three to five minutes, and then wash in water, not allowing it to remain for more than a couple of seconds, but rapidly transferring it to acidulated water (eight drops of acetic acid to a basinful of water). This last part of the operation must never be neglected, as the carmine is held in solution by an alkaline fluid,

and is only precipitated in the tissues when the fluid is rendered acid. Where the stain is properly selective, the nuclei and fully formed fibrous tissue are stained carmine and a delicate pink respectively; other formed material remains unstained, or is only slightly tinted. The axis cylinders of medullated nerve fibres are stained a brilliant carmine colour, as are also the nerve cells of the cord, &c., but here not so deeply. A more selective stain is obtained by staining the sections slowly in a watery solution of the above. The sections are afterwards treated in the same way. The sections so stained may be mounted in glycerine or Farrant's solution (§ 97, p. 70), or when it is wished to clear up the section still more, it may be mounted in Canada balsam (§ 100, p. 72).

76. *Methylaniline violet* is one of the most useful of the aniline dyes, especially to the pathological histologist, as it gives with certain normal tissues a double stain; with tissues in which there is waxy degeneration it differentiates the affected parts most clearly. It may be used as a strong watery solution, but by far the best and most reliable preparation is the Telegraphen Tinte, prepared by A. Leonhardi of Dresden. The sections to be stained are placed in a watch-glass, with about half a drachm of the staining fluid of the watery solution of either the ordinary aniline or of the ink. The strength should be such that when held up to the light in a three-quarter inch test tube it permits the light to pass pretty readily. Leave them for two or three minutes; then wash well for half an hour in water, and mount in glycerine, either pure, or, according to Cornil, slightly acidulated with acetic acid. Farrant's solution may also be used as a mounting medium. With any of the above media the staining is pretty permanent. Do not use dammar or Canada balsam, as both the clove oil and alcohol dissolve out the colour, and even the chloroform which is used as a solvent for the dammar or balsam dissolves out the methylaniline pretty readily, so that the colour, in some cases especially, is gradually discharged from the tissue, as where the section has been imperfectly washed, and is diffused over the section, which then becomes blurred and muddy looking. It gives two reactions, a red violet and a blue violet; these are very well seen in hyaline cartilage, where

the matrix takes on the red violet stain, and the cells the blue violet; or again, in "waxy degeneration," where the "waxy" material takes on the red violet stain, whilst the healthy tissues take

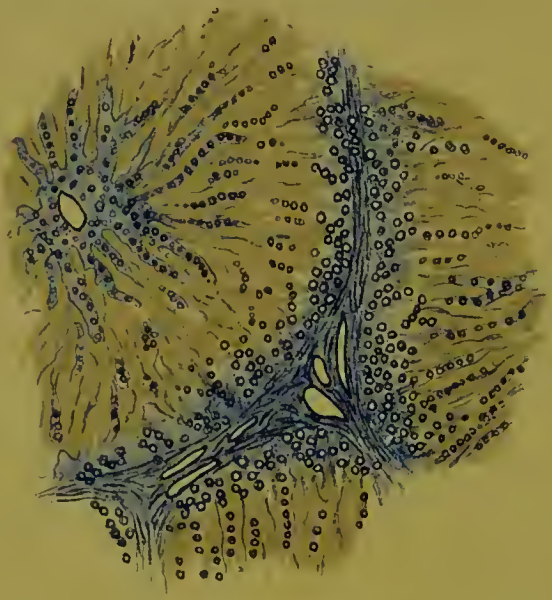


FIG. 4.—Section of waxy liver stained with methylaniline violet— × 70 (after Thierfelder). Waxy material stained red violet. Normal and fatty tissue stained blue violet or slaty blue.

on a blue colour, in some instances almost a slaty blue (Fig. 4). If it is not convenient to mount them all at once, these stained specimens may be kept for any length of time in preservative fluid (§ 71, p. 52). They cannot be kept in alcohol, as it discharges most of the colour from the tissues, and what staining remains is too diffused. For fresh tissues, epithelial structures, salivary corpuscles, or cells from the vagina or urethra, it is extremely useful. Used as a dilute watery solution (one or two per cent.), it brings out nuclei and connective tissue corpuscles. These tissues should be mounted in "a saturated watery solution of potassic acetate." This preparation is also useful as a staining reagent for micrococci and bacteria, as these organisms take up the stain and keep it, even when the tissue is washed in alcohol; so that sections containing such organisms may be mounted in glycerine or Farrant's solution, after they have been well washed in very dilute acetic acid, or they may be washed in alcohol, rendered more transparent in clove oil, and then mounted in dammar mounting fluid or Canada balsam (§ 100, p. 72).

77. *Iodine staining solution* is made by adding water to tincture of iodine until it is about the colour of a very dark sherry or a brown vinegar. It should never be very strong for microscopic staining. This reagent is of value in staining "waxy" tissues, which it colours a rich mahogany brown when the section is examined by reflected light, the normal tissues appearing yellow. When examined by transmitted light, however, the waxy material appears to be a lighter yellow than the surrounding healthy tissues, as it is much more translucent. In connection with this staining it is to be remembered that the granules of glycogen in liver cells are stained the same mahogany brown colour, as are also some of the cells in growing bone. To stain a section place it in a watch-glass, and pour over it a small quantity of the solution; allow it to stand for ten minutes; wash rapidly in water, and mount in iodine mounting fluid (see below)—never in Farrant or glycerine, or the staining soon fades, as the iodine diffuses into the fluid. Another method which may be used. The section may be floated out on the slide, and a small quantity of the fluid dropped on with the glass rod; this is allowed to stand for a few minutes, and then a drop of the mounting fluid is added, and the cover glass lowered on to the specimen. Where iodine is used the solution in which the section is mounted must be kept saturated with iodine, and as this is very volatile, the cover glass must be cemented down at once with French glue, or some substitute.

To make the iodine mounting fluid, take of

Liquor iodi. (B.P.)	3½ parts.
Glycerine	6 parts.
Water	6 parts.
Mix, and add, carefully picked gum arabic, about	6 parts.

Keep in a stoppered bottle, stirring or shaking regularly until the whole of the gum is dissolved. Allow the fluid to stand until all air bubbles have risen to the surface, and then decant into a small stoppered bottle to which a glass rod is fused (§ 31, p. 27). This fluid is used as a preserving medium only where sections are stained with iodine.

78. To obtain the blue reaction with *iodine and sulphuric acid* in waxy organs, treat the sections in a test glass with a sherry coloured watery solution of iodine for about half an hour; then immerse them in a four per cent. solution of sulphuric acid until the blue colour makes its appearance. Mount in glycerine (§ 97, p. 70), or Farrant's solution (§ 98, p. 71). This is an extremely delicate test for waxy material, but unfortunately it succeeds only in some cases, though in the hands of some observers extremely satisfactory results have been obtained.

79. *Eosine* used as a one-tenth per cent. solution gives a beautifully transparent stain, and one which will remain unaltered for a considerable length of time. It may be used as a watery solution, especially for muscular tissue of the heart, &c., or as an alcoholic solution for staining the coloured blood corpuscles. It stains nuclei pink, but these are better brought out by exposure to the action of the log-wood staining fluid (§ 74, p. 56), for a few seconds after staining with the eosine.

To stain with eosine, filter a few drops of the solution into a watch-glass, place the sections in this, and allow them to remain there for about a quarter or half a minute. Wash them in water slightly acidulated with acetic acid. Mount in Farrant's solution (§ 98, p. 71), acidulated glycerine (§ 97, p. 70), or balsam (§ 100, p. 72).

80. *Osmic acid* is perhaps the most delicate of all staining reagents, and is invaluable for staining fat and nerve fibres, in addition to which it is frequently used as a hardening reagent. It may be kept as a one per cent. watery solution, made by breaking the glass tube in which it is supplied in a mortar, and triturating with one hundred parts of distilled water. It is to be kept cool in a glass-stoppered bottle, well protected from the light by a covering of brown paper closely gummed to the bottle. It may afterwards be diluted as required.

As a hardening reagent, it is extremely useful for *small* pieces of delicate tissue, such as nerve fibres, retina epithelium, and the like, for which purpose it is used as one-sixth to one-half per cent. solution. The tissue is allowed to remain in it for about six or eight hours, or

even longer, according to the size and nature of the piece of tissue, carefully protected from the light. Wash well in distilled water, after which the tissue may be transferred to the gum and syrup solution, frozen, cut (§ 67, p. 48), and mounted in Farrant's solution, (§ 98, p. 71).

Osmic acid appears to tan the tissue, fixing the tissue elements without producing a granular precipitate, or causing shrivelling (Rutherford). When used as a staining reagent it is used as a one-twelfth to one-sixth per cent. solution. The sections to be stained are placed in a small quantity of the fluid carefully protected from the light, and left for from one to twelve hours. They are then taken out and washed in distilled water, and mounted in Farrant's solution (§ 98, p. 71), or glycerine (§ 97, p. 70); never in Canada balsam or dammar. This staining reagent blackens fat, the myeline of white nerve fibres, the outlines of fibres and cells, at the same time staining the substance of these structures a greenish grey or olive green colour.

81. *Aniline blue black* is especially useful for staining sections of the nerve centres, in which it brings into special prominence the nerve cells, which are stained a slaty blue colour. (Bevan Lewis.)

It is made as follows:—Take of

Aniline blue black	1 part.
Water	40 parts.
Dissolve and add rectified spirit . .	100 parts.

Keep in a stoppered bottle, filter a few drops into a watch-glass, and add eight or ten times as much alcohol to it. Stain the section from a half to three minutes, and mount in Canada balsam (§ 100, p. 72). For ordinary tissues use a one per cent. watery solution, allow the sections to remain in it for a few minutes, and then mount in balsam. If the staining is too deep, Stirling recommends soaking the sections for a time in a two per cent. solution of chloral hydrate.

82. *Gentian violet*, as recommended by Weigert for staining tubercle bacilli, is prepared by adding a two per cent. watery solution of gentian violet twelve parts, with saturated solution of aniline oil water one hundred parts.

To prepare this saturated aniline oil water, take of

Aniline oil	1 part.
Distilled water	3 parts.

Shake well every half hour for three or four hours, and decant the water as the oil settles to the bottom. For this solution the commercial aniline answers quite as well as the pure, and is about a twelfth of the price. For ordinary staining with gentian violet, a two per cent. watery solution, to which is added a crystal or two of thymol dissolved in alcohol, may be used. When mounting in balsam, do not leave the section too long in either the alcohol or the oil of cloves, both of which reagents dissolve out the staining fluid very rapidly.

83. *Magenta* is not a very permanent stain, but it may be used especially for staining fresh tissues, for blood corpuscles, and, by Heneage Gibbes's and Ransome's methods, for the bacilli of tuberculosis, &c.

For ordinary tissues, dissolve one twentieth part of magenta in one hundred parts of ten per cent. solution of alcohol.

For blood corpuscles, dissolve one part of magenta in one hundred parts distilled water and one hundred parts glycerine.

This stains the nuclei of the white blood corpuscles a somewhat deep magenta colour, the protoplasm taking on only a faint tinge of the same colour.

GIBBES'S FORMULA.

Magenta crystals	2 parts.
Pure aniline	3 parts.
Alcohol (sp. gr. ·830)	20 parts.
Distilled water	20 parts.

[1] "Dissolve the aniline in the spirit, triturate the magenta in a glass

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[1] Gibbes's modified method (see the *Lancet*, May 5th, 1883) gives very good results. Take of

Rosaniline hydrochloride . . .	2 grammes.
Methyl blue	1 gramme.

Triturate in a glass mortar.

Then dissolve aniline oil . . .	3 C.C.
in rectified spirit . . .	15 C.C.
Slowly add distilled water . . .	15 C.C.

Keep in a stoppered bottle. Treat the sputum in the ordinary way, warm the fluid

mortar to a fine powder, add the spirit gradually while stirring, until all the colour is dissolved, then add the water slowly, still stirring, and put in a stoppered bottle."

84. RANSOME'S FORMULA.

Pure aniline	3 parts.
Alcohol anhyd.	42 parts.
Magenta or fuchsin	1 part.
Distilled water	45 parts.

Mix and preserve as above.

85. *Fuchsin.*—A concentrated watery solution of acid fuchsin should also be prepared by those who intend to investigate the pathology of the nerve centres. The method of staining these tissues with fuchsin will be referred to under the heading of diseases of the nervous system, and the various methods of staining bacilli will also be more fully described each under its appropriate heading.

86. Ehrlich's formula for staining tubercle bacilli :—Take of

Pure aniline	5 parts.
Distilled water	100 parts.

"Shake well and filter through a moistened filter; to this add a saturated alcoholic solution of fuchsin, methyl violet or gentian violet, till precipitation commences." The rapidity of staining varies with the temperature.

87. *Bismarck brown*, prepared as follows, is an exceedingly useful contrast stain, and is also invaluable for staining sections of bone and young granulation tissue. Take of

Aniline brown	1 part.
Alcohol anhyd.	10 parts.
Distilled water	100 parts.

The sections must be stained slowly, and the water in which the

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gently, transfer the cover glass to the warmed fluid, allow it to remain for four or five minutes, "wash in methylated spirit until no more colour comes away, drain thoroughly, and dry either in the air or over a spirit lamp. Mount in Canada balsam." Sections may be stained in the same fluid in three or four hours. No nitric acid is used.

staining fluid is suspended must contain about ten per cent. of methylated spirit. Make a straw-coloured solution, and allow the sections to remain in this for several days. Mount in Canada balsam (§ 100, p. 72). Where used as a contrast stain, pour a few drops of the strong solution into a watch-glass, and allow the section to remain in this for about ten minutes. This gives a very transparent brown colour to the nuclei and the margins of the cells, leaving the protoplasm almost unstained.

88. *Chrysoidin* is chiefly used as a contrast colour, but it is gradually being superseded by methylene blue. Gibbes recommends a saturated watery solution of chrysoidin, to which is added a crystal of thymol dissolved in alcohol.

89. *Methylene blue* is used as a contrast stain, and is also a very good stain for muscular fibre.

To prepare a saturated solution of methylene blue, take of

Methylene blue	1 part.
Alcohol anhyd.	15 parts.
Distilled water	35 parts.

When the fluid is to be used, dilute with about five times its volume of water. Mount muscle stained by this method, in glycerine (§ 97, p. 70), or Farrant's solution (§ 98, p. 71).

90. *Iodine green.*—This should properly have been taken up along with methylaniline violet, as it is principally for its reaction with waxy material that it is used by the pathologist. As a one per cent. watery solution, it gives a beautiful rose pink reaction with waxy material, staining the normal tissue a bluish green colour. Mount in Canada balsam (§ 100, p. 72), but remember that alcohol dissolves out this colour very rapidly, hence the section should not remain very long in this fluid, nor should it remain long in the clove oil, which also quickly discharges the colour.

91. *Gold chloride* is of comparatively little use to the pathologist, except in the case of tissues which can be transferred at once to the staining fluid. In the examination of the morbid conditions of the

cornea, it is, however, an extremely valuable reagent, as also in the cases of nerve terminations in muscles which have been removed from the body during life. It is to be remembered that it can be used only within a quarter of an hour of the removal of the part from the living body. It may be used in either of the following ways :—

(*a.*) Soak the tissue as soon as removed from the body in a half per cent. solution of chloride of gold, until it assumes a lemon colour; then expose in one per cent. acetic acid solution to strong light, until it assumes a purplish tinge. Sections when made show connective tissue corpuscles (corneal corpuscles, cartilage cells), nerve fibrils, especially those of small size, and ganglion cells stained a reddish purple colour. Mount in glycerine (§ 97, p. 70).

(*b.*) Ranvier's method gives extremely good results; its only disadvantage is that, during the process, epithelial cells are removed. It is especially useful for staining nerves, &c. in dense tissue.

Filter the juice of a lemon through clean starchless muslin. Soak small pieces of perfectly fresh tissue in this for about five minutes; wash out the lemon juice with distilled water, and then transfer to a one per cent. solution of gold chloride, in which allow it to remain for half an hour. Again wash in distilled water, after which keep in a stoppered bottle, carefully protecting from every ray of light for twenty-four hours, during which period the tissue should be exposed to the action of a twenty per cent. solution of formic acid. At the expiration of this period the same purple colour will have appeared. Wash again in distilled water, and preserve in glycerine (§ 97, p. 70).

92. *Nitrate of silver* is used specially to bring out the intercellular substance, in which it is reduced by light to the black oxide of silver. It is also used as a stain for the intercellular substance of cartilage, and for the laminated intercellular tissue of the cornea, though, if the tissues be exposed for a considerable time in the silver solution, the nuclei, and even the protoplasm of connective tissue, epithelial or fat cells may become more or less blackened. To the pathologist it is

specially useful in the study of the eye and of tumours of epithelial type, as most other tissues have been dead for some time before they come into his hands. For demonstrating the structure and relations of the alveoli of cancerous growths, this reagent is perhaps the most valuable at command. Take a very thin section of the tissue to be stained as soon as it is removed from the body, and wash well in distilled water to remove all chlorides, which would at once throw down the silver as a white precipitate. Expose it to the action of a large quantity of half per cent. solution of nitrate of silver for from five to ten minutes (until it becomes somewhat whitened); wash in water (not distilled), and expose to diffuse daylight until a delicate brown colour makes its appearance. Care must be taken to protect the specimen from the direct action of the sun's rays, or the tissues become quite opaque and stained. Preserve these specimens (if not mounted at once) in a mixture of glycerine two parts and water one part, to which are added five to ten drops of acetic acid to each ounce of the mixture. Mount in glycerine(§ 97, p. 70).

Other Reagents used in the Preparation and Mounting of Sections.

93. *Acetic acid.*—One part glacial acetic acid to four parts water is extremely useful for dissolving albuminoids, and for bringing the nuclei of cells into special prominence, as in the case of pus corpuscles or white blood corpuscles. It is used in the same way for making sections of tissue more transparent, such as lymphatic glands, or the spleen, in which cases it also acts by dissolving the albuminoids and bringing certain structures into greater prominence. A stronger solution is used to neutralise logwood where the stain is too deep (§ 74, p. 58), and a weaker solution (one drop to the ounce) to fix carmine in the tissues by precipitation (where strong carmine is used as a rapid staining reagent) before the sections are washed and mounted.

Beale's mixture of glycerine one ounce and glacial acetic acid five drops may also be used for clearing up tissues as above.

94. *Caustic potash or soda,* forty per cent. solution, is also extremely useful for clearing up sections of fresh tissues, or any tissues which

are to be mounted in glycerine or Farrant's solution, both of which fluids also increase somewhat the transparency of tissues, as they have a higher refractive index than water. Reference has already been made to its use in separating muscular fibres (§ 66, p. 47).

95. *Bicarbonate of soda*, five per cent. solution, is principally used for neutralising the acid, hardening fluids (picric acid or chromic acid) before using staining reagents, such as logwood. They must be thoroughly neutralised by using a weaker solution than the above after the sections are cut. The staining may then be proceeded with.

Fluids used in Mounting Sections.

96. *Clove oil or turpentine* is generally used to render stained tissues more transparent before they are mounted in Canada balsam or dammar varnish. Clove oil is the more powerful of the two, and is more frequently used, as it is also much more agreeable to work with; but, as already found (§ 76, p. 60), it is a powerful solvent of aniline colours, so that where the tissues are stained with these dyes, turpentine is used instead of the clove oil, as in the mounting of tubercle bacilli. Before the oil of cloves can be applied to the section, all water must be abstracted, which is done by means of absolute alcohol. The method of procedure is much as follows:—After staining the section, wash well in water to remove all the staining fluid not actually taken up by the tissues; pour about a drachm of absolute alcohol into a watch-glass, and a similar quantity of clove oil into another; take the section from the water with a needle, and remove as much of the water as possible by means of a piece of blotting paper or a soft cloth, allowing the free end of the section just to touch one of these absorbent tissues; place the section in absolute alcohol, allow it to remain there for two or three minutes without attempting to spread it out; transfer the section with a dry needle to the oil of cloves, when the alcohol, rapidly diffusing into the clove oil, carries the edges of the section with it, and in this way the section is spread out on the surface of the clove oil. It must not be left for an instant after it is clarified—(this should never take longer than half a minute if the section has been properly dehydrated),—as the

clove oil renders the tissue extremely brittle and friable. To transfer the section from the clove oil to the slide, pass the blade of the copper lifter, after carefully oiling it, under the section as it is spread out on the surface of the oil of cloves, then fix one margin of the section with the point of a needle and lift up; have the blade as nearly horizontal as possible, so that the section still floats in oil on the blade; bring the blade down on to the slide, *which must be perfectly dry*, and, fixing the edge of the section with the point of the needle, gently *withdraw* the copper lifter, leaving the section on the slide. Tilt the slide to allow any superfluous oil to drain off, dry carefully with a soft cloth, put on a drop of Canada balsam or dammar varnish, lower a cover glass on to the section and press it down with the handle of the needle—any air bubbles which may have become entangled in the section being by this means driven out. In a day or two the cover glasses become perfectly firm, and will bear any amount of knocking about.

97. *Glycerine*, or some fluid in the composition of which glycerine is an important element, is the most useful fluid for the preservation of thin sections which are to be transferred at once from the water to the slide. Where the pure glycerine alone is used, as for extremely delicate tissues, thin sections of lung, or peritoneum, the section is placed on the slide (§ 38, p. 33), superfluous moisture drained away or removed with a soft cloth, and then a small drop of glycerine dropped on to the section with a glass rod: the size of this drop can only be determined experimentally, but it is always better to err on the side of too large a drop, as air bubbles are not then such frequent intruders under the cover glass. Let fall the cover glass on to the section (§ 33, p. 30), and press down gently with the handle of the needle to expel air bubbles, which with glycerine only too frequently get in, and are then very difficult to drive out. All superfluous glycerine at the margin of the cover glass must be removed with the aid of a small glass pipette, or a brush slightly moistened, and then the slide should be carefully dried with a soft cloth, and cemented in the course of an hour or two. The advantages of glycerine as a mounting fluid are its simplicity and its clarifying property, especially for sections unstained, or stained with the metallic staining reagents, and

more particularly those tissues which are to be examined with high powers. It disadvantages are, that it does not dry at all, and so does not fix the cover glass, that it sometimes clears up sections too much, and also that it causes fresh white fibrous tissue to swell up and look almost gelatinous. In place of glycerine, Farrant's gum and glycerine fluid is now generally employed.

98. *Farrant's Mounting Fluid.*—Take of

Water,
Glycerine,
Arsenious acid, saturated solution (saturated by boiling), . . . equal parts.

Mix well in a covered jar, and add about half the bulk of picked gum arabic; allow these to stand for three weeks, stirring daily, or until the whole of the gum is dissolved. Then filter through coarse filtering paper, or allow it to stand for a further period of a couple of weeks, when the air bubbles will have come to the surface, and any dirt will have settled to the bottom. Decant into a one-ounce stoppered phial, to the stopper of which a glass rod is fused. Use in same way as glycerine. If too much gum be used, the tissues are apt to become slightly granular, whilst if too much glycerine be used the tissues become transparent, the Farrant's solution does not dry, and the cover glass remains unfixed.

This is one of the most useful of all the media for preserving sections for microscopic examination. It combines most of the advantages of glycerine with few of its disadvantages. It does not cause fresh tissues to swell so much, and does not render sections quite so transparent, though it does clear up the section, especially after it has been mounted for a few days. It also acts as a preservative medium, on account of the presence of the arsenious acid; and the glycerine, by its affinity for water, keeps the section moist, the only part at which the fluid dries being at the edge of the cover glass. By this drying the cover glass is fixed slightly by the gum, and after the specimen has been mounted for two or three days, the slides may be cleaned, and the cover glasses cemented with Hollis's glue, india-rubber solution, or gelatine solution. The great disadvantage about this fluid is that sections kept in it for a number of years become cloudy and granular looking.

99. *Camphor mounting fluid* is sometimes used in place of Farrant's solution, in preparations where the arsenious acid might affect the staining or injecting fluid with which the tissue is impregnated. For instance, sections taken from an organ injected with Prussian blue must be mounted in a fluid which contains no arsenious acid, as that substance causes decolorisation of the iron blue.

The fluid named consists simply of Farrant's solution, in which the arsenious acid is replaced by camphor water. Take of

Camphor water	2 parts.
Glycerine	1 part.
Pure picked gum arabic . . .	1½ parts.

Prepare in the same manner as Farrant's solution, and then keep a piece of camphor floating in the fluid. Use it in the same manner as glycerine or Farrant's solution.

Canada Balsam and Dammar Varnish.

100. These mounting fluids may both be used for deeply stained sections, especially where it is necessary to bring into strong relief the stained parts of tissue. They can be used only where the tissues have been previously dehydrated, and then cleared up with some substance with which they will amalgamate. Each fluid has its special admirers, and each has its special advantages, the disadvantages being that Canada balsam has a somewhat yellow tint, and hence is not fitted as a mounting medium for sections which it is intended to photograph, but the sections so mounted keep perfectly well for years. Sections mounted in dammar varnish as a rule become somewhat cloudy and granular after they have been kept for a year or two; but when fresh they are beautifully transparent, and the medium itself is perfectly free from colour, so that it is admirably adapted for photographic work. To prepare Canada balsam mounting fluid, heat the ordinary Canada balsam gently for about twenty-four hours in a covered vessel; allow it to cool to a yellow vitreous looking mass; take of this 100 parts.

Chloroform . . .	47 ,,
Turpentine . . .	47 ,,

Dissolve the Canada balsam in the chloroform and turpentine, and

filter through fine cotton wool. It must be kept in a stoppered bottle which has previously been carefully dried, and rinsed out first with absolute alcohol, and afterwards with turpentine or benzole. It must also be kept in a dry place.

If the Canada balsam is to be used for mounting stained bacteria, especially tubercle bacilli, the chloroform must be replaced by benzole, which is not nearly so powerful a solvent of the aniline colours as is the chloroform.

101. Dammar varnish is prepared as follows :—Take of

Gum dammar	2 parts.
Gum mastic	1 part.
Turpentine	4 parts.
Chloroform	2 parts.

(These proportions may vary somewhat as a thinner or a thicker fluid is preferred, but the above proportions give very good results.)

Mix in an earthenware jar, stirring and agitating until the gums are dissolved, and then filter through coarse filtering paper into small stoppered phials, to the stoppers of which glass rods have been fused.

Cementing of Cover Glasses.

102. For this purpose various solutions have been suggested, but the same great difficulty almost invariably presents itself, that with almost all these substances the glycerine sooner or later leaks out. With Farrant's solution there is not the same danger, so that it is sufficient to run a ring of gold size, French glue, Hollis's marine glue, or indiarubber solution around the margin of the cover glass, after carefully cleaning the slide, and allowing the gum in the Farrant solution to partially fix the cover glass. It is then left for twenty-four hours, after which a ring of zinc white cement is laid over the ring already put on, and this may be repeated in the course of a day or two, when the first layer has become properly set.

103. This zinc white cement is composed of

Benzole	8 parts.
Gum dammar	8 parts.
Oxide of zinc	1 part.

Mix the gum dammar and the benzole, filter through cotton wadding, after which mix in the oxide of zinc in a mortar, and again filter through the wadding.

This cement forms a very workable material, and when set it is as hard and firm as enamel.

Slides cemented in this manner will, if properly done in the first instance, keep perfectly free from leakage for years.

104. For sections mounted in glycerine undoubtedly the best method is Dr. Marsh's, who suggests gelatine solution as a cement for first fixing the slide; the reason for this is that gelatine readily mixes with the glycerine in its immediate neighbourhood.

He prepares the solution by placing a small quantity of gelatine in a narrow glass beaker, covering it with water, and allowing the gelatine to take up as much of the water as it will. Any superfluous water is poured off, the mixture is heated, and three or four drops of creosote are added to each ounce of the fluid; keep in a small bottle, and each time that the mixture is needed, it is "rendered fluid by immersing the bottle containing it in a cup of warm water." The slide must be perfectly freed from glycerine by the aid of a camel hair pencil and a damp cloth. A ring of the gelatine fluid is painted round the edge of the cover glass. As soon as this is set, paint it over "with a solution of bichromate of potash, made by dissolving ten grains of that salt in one ounce of distilled water." He recommends that "this application of bichromate of potash should be made in the daytime, as the action of daylight upon it, in conjunction with the gelatine, is to render the latter insoluble in water;" wash well in methylated spirit to remove all the glycerine, and then run on a ring of zinc white, which may be repeated until a good firm ring is made.

105. In applying these rings, it is well to use a "turn-table." This is a heavy brass disc about three inches in diameter, which should work smoothly on a conical pointed pivot fixed to a solid piece of wood. On the disc may be marked or engraved a series of concentric rings, each of which should correspond in size to the size of a cover glass. Then a couple of brass clips are affixed, which serve

to keep the slide in position when the cover glass is "centred." With a goat hair brush lay on first a ring of the size or other cement, and when this is dry, put on the zinc white. In working with the cements always keep the brushes clean. This is done by means of warm water for the size, glue, or gelatine, and turpentine or benzole for the zinc white. When the zinc white becomes too thick to run readily, it may be diluted with benzole.

106. Label the slides with the name of the tissue, the disease, date, method of staining and mounting employed, and the date of mounting. It is ready for future examination, and should be kept in the flat trays already spoken of (§ 30, p. 27), carefully protected from both light and dust.

CHAPTER III.

THE LIVER.

107. The weight of the normal liver when taken from the body should be about 3 lbs., more or less. The surface is smooth, and the capsule has a glistening appearance, is of a bluish pink colour, and is fully though not tensely distended. This glistening appearance is due to a reflection of the peritoneum over the surface of the organ, and is not to be seen at the posterior border, where the peritoneum is absent.

Beneath the capsule, and through the delicate subcapsular tissue, the lobules or small subdivisions of the liver substance can, as a rule, be made out, varying in size from about 1-20th to 1-16th of an inch in diameter. On making a section the substance cuts readily, but is

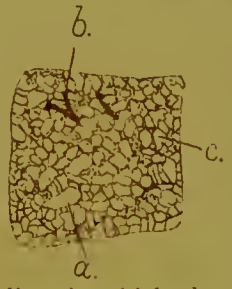


FIG. 5.—Taken from a liver in which there was fatty degeneration (where the outlines of the lobules are more distinctly marked). The size of the lobules is here indicated. The larger openings (*a*) are transverse sections of vessels, the dark lines (*b*) bands of fibrous tissue in portal spaces. The smaller openings (*c*) correspond in size to the lobules of the liver.

firm and close ; the surface of the section is of a dull chocolate colour, and here again the outlines of the lobules of a healthy liver may be indistinctly made out. The capsule is exceedingly thin and delicate, and only here and there may be seen very delicate bands of connective tissue passing into the deeper part of the liver substance. In the cut section, too, may be seen a number of large openings, which are mostly the branches of the portal vein. The gall bladder as a rule is semi-

distended with a brownish yellow coloured bile, which may be readily pressed through the common duct into the duodenum.

108. To prepare such a liver for microscopic examination, the tissue is cut into small blocks, not more than three-quarter inch cubes, or one inch square and half an inch thick; one or two at least of these being from the surface of the liver, in order that there may be a piece of the capsule for examination. Half a dozen of these pieces are placed in Müller's fluid (twenty vols. to one of tissue) in a wide-mouthed bottle, which is to be kept in a cool, dark place. At the end of twenty-four hours the fluid is poured off, the blood is washed from the jar and cubes, and fresh fluid is added. This fluid is again changed at the end of the first and third weeks, after which the tissues may be preserved in methylated spirit, after soaking in water and weak spirit (§ 53, p. 43). Cut sections (§ 67, p. 49). Stain a section with picro-carmine (see § 73, p. 54), and examine.

109. It will now be well to examine carefully in order the capsule, the portal vein, the hepatic artery, the hepatic vein, the bile ducts, and the liver cells, or parenchyma of the organ. With the capsule must be examined the inter and intra-lobular connective tissue.

On the outer surface of the capsule is a layer of endothelial cells; beneath this serous layer proper is a layer of irregular connective tissue, in which are yellow elastic fibres, and, deeper still, a more or less lamellated layer of connective tissue, known as a continuation of Glisson's capsule. It is this capsule of Glisson which plays such an important part in certain conditions such as perihepatitis and poly-lobular cirrhosis. Continuous with the subcapsular tissue are processes of similar lamellated tissue running at intervals into the substance of the liver, where they are again met with in the portal canals. Between the lamellæ are a number of flattened branching connective tissue cells. In the human liver the interlobular tissue is comparatively scanty between individual lobules, but connective tissue is found in considerable quantities running along with the larger branches of the portal vein. Before going further, it will be well to say that a study of a single lobule of the liver, and a single portal canal, will give the key to the structure of the whole organ.

The portal canals are the large spaces in the liver, in which are seen the openings of the branches of the portal vein. In one of these canals are



FIG. 6.—Contents of portal canal of dog. (Klein and Noble Smith.)

V.P. Section of the portal vein, a large lumen and comparatively thin wall.

a. The small branches of the hepatic artery, with their thickened walls.

b. Sections of bile ducts with the regular layer of nucleated columnar epithelium and the small orifices.

c. Connective tissue supporting the various structures in the canal.

found—(1.) A large opening (*V.P.*), the portal or interlobular vein, which brings the blood from the alimentary tract to the stomach. The walls of this vessel are comparatively thin. (2.) One or two small branches of the hepatic artery (*a*) with thick walls. These arterioles have the structure of small arterioles, as seen in any other part of the body. (3.) Two small bile ducts (*b*) in which the walls are of considerable thickness in comparison with the lumen of the tube, and lining the thick wall is a distinct layer of nucleated columnar epithelium.[1] (See structure of epithelium of bile duct, p. 104, § 118.) Around these various structures there is a considerable quantity of connective tissue (*c*), which has entered the liver at the hilus, along with the vessels, and now leaves

[1] It will be well to remember the distribution of these vessels when the search for a lobule is entered upon. To find a lobule, look first for several portal spaces, which may be recognised by the fact that they contain *several* openings. Draw imaginary lines from these spaces to a common centre. Near this centre will be found a *single* opening—the hepatic vein, the centre of a lobule. The periphery of this lobule is marked by lines running at right angles to those drawn towards the centre, joining the several portal spaces.

these portal canals to run in the smaller portal spaces, and between the lobules, to meet the bands of connective tissue which are continuous with the deeper layer of the capsule on the surface of the liver. In this way is formed a supporting framework for the liver substance proper. Examine a section through a lobule near the portal canal. It may be considered as a mass of polyhedral cells arranged around a central vein, a branch of the hepatic vein. Piercing this mass of



FIG. 7.—Diagramatic representation of the structure of a small portion of the liver, altered from Quain's "Anatomy."

S.V. Sublobular vein, into which the central veins, or hepatic venules, *C.V.*, open.

I.F. Interlobular fissure, in which run the portal vein, &c. ; and running from the portal vein to the central vein are the portal capillaries, *P.C.*

P. The parenchymatous tissue, or gland substance proper, composed of masses of polyhedral cells.

cells, and running from the portal vein at the periphery towards the centre, are numerous capillary vessels, bringing the blood into very close contact with the liver tissue proper. Around these vessels are numerous lymphatics, which play a not unimportant part in the changes occurring in certain morbid conditions. Between individual cells, or rather at the angles between several cells, are the bile capillaries, which in their most minute ramifications are simply channels between adjacent liver cells. These open into the bile ducts

by a gradual modification of the liver cells into an epithelial layer. Fig. 8.

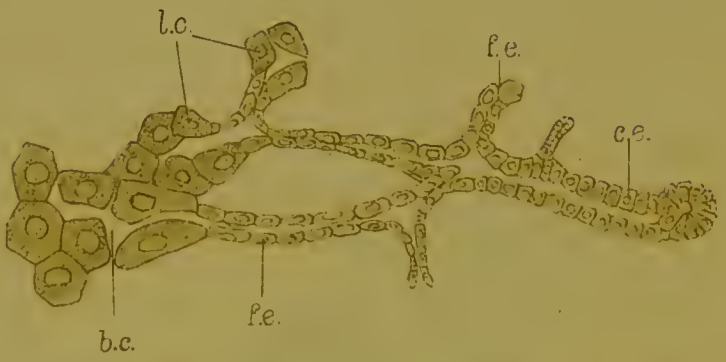


FIG. 8.—Commencement of biliary channels, and structure of smaller bile ducts (after Klein and Noble Smith).

b.c. Biliary canaliculi in the angles between adjacent liver cells.

l.c. Liver cells, slightly modified, just before the commencement of the bile duct proper with its lining of flattened epithelium, *f.c.* (intermediary portion of the duct).

c.c. Cubical epithelium of the somewhat larger bile duct.

The lobules are arranged in groups, and the central veins of one of these groups open into a larger branch of the hepatic vein spoken of as the sublobular vein (Fig. 9). When a tranverse section,

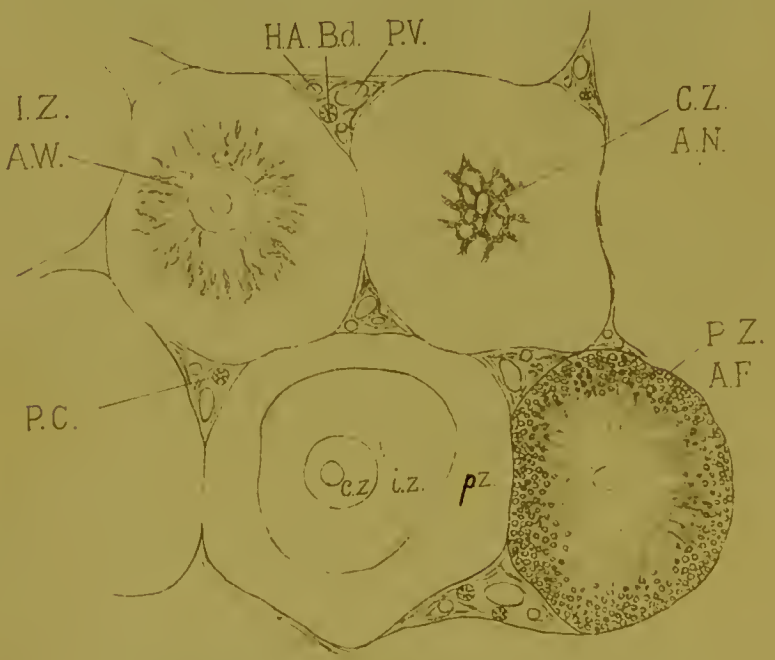


FIG. 9.—Diagramatic representation of lobules of the liver, divided into zones.

P.C. Portal canal, in which are contained the following structures:—*B.d.* Bile duct. *V.P.* Portal vein. *H.A.* Hepatic artery. *C.Z.* Central zone. *A.N.* Area in which chronic venous congestion is first manifested. *I.Z.* Intermediate zone. *A.W.* Area in which waxy change is met with. *P.Z.* Portal or peripheral zone. *A.F.* Area of fatty infiltration.

through one of these groups of lobules is examined, there is the arrangement seen in Fig. 9. The following structures are cut through :—(1.) those situated at the angles between the lobules (in the portal space, Fig. 2); and (2.) the mass of liver cells perforated by the various structures already mentioned, including the hepatic or intra-lobular vein. For pathological purposes this section is mapped out into three distinct zones, each of which is specially affected by a particular series of lesions. These are—*1st.* The peripheral or portal zone, which, as its name indicates, is situated at the periphery of the lobule, and occupies one-third of the diameter of the section; *2d.* Within this is the intermediate zone, or, as it is sometimes named, the zone of the hepatic artery, which, roughly speaking, also occupies one-third of the diameter. It is named the zone of the hepatic artery from the fact that the venous capillaries of the hepatic artery are supposed in this region to empty their contents into the portal *venous* capillaries which run between the inter- and intra-lobular veins. *3d.* And lastly, there is the central zone, or that of the hepatic vein, situated in the centre of the lobule. At the periphery of the lobule are the small branches of the portal vein, which empty their blood into the intercolumnar or portal capillaries. As Klein points out, there are, in consequence of the mass of liver cells being *pierced* by the portal capillaries, some short transverse masses of the liver cells running at right angles to the radiating columns of the cellular net-work. The liver cells making up these columns are polygonal in shape, and have an extremely granular appearance; as a rule a single oval nucleus is to be observed, which stains deeply with carmine, &c., and there is a cell wall to be demonstrated.—(Haycraft.) Throughout the cell, granules of glycogen and brown pigment are seen, whilst in a liver removed from an animal killed shortly after food has been taken, globules of fat may also be noticed in the cells of the peripheral zone. The granular appearance of the protoplasm is due to the existence of an intranuclear and an intracellular plexus, to be made out only with the aid of a very high magnifying power.

Cloudy Swelling of the Liver.

110. This is a condition which should be specially looked for in organs taken from patients who have died during the course of certain

acute febrile conditions (yellow fever), especially those of septicæmic origin, or scarlatina, small-pox, &c., and in the early stages of phosphorous, arsenic, antimony, alcohol, or sulphuric ether poisoning.—(See Fatty Degeneration, § 113, p. 86.)

The liver in such a condition is found to be swollen, and the capsule comparatively tense; the organ is somewhat paler than normal, as the amount of blood in the *capillaries* appears to be diminished, and the whole organ, instead of having a clear glistening appearance, is somewhat opalescent looking. Preserve for examination (§ 54, p. 43), stain in picro-carmine (§ 73, p. 53).

Examine under the low power (× 50).—The lobules are rather more distinctly marked out owing to a slight increase in the number of

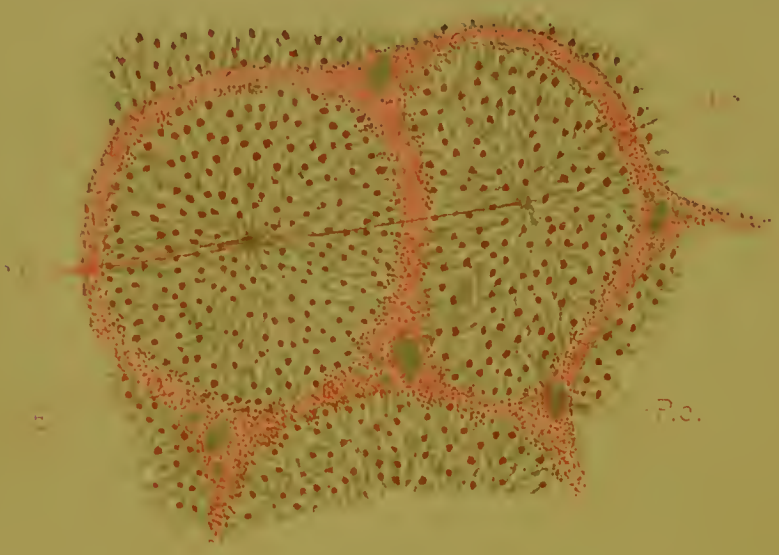


FIG. 10.—Drawing of cloudy swelling of the liver, with interlobular small cell exudation. Stained in picro-carmine. (× 50.)

C.v. Central or hepatic vein—small, in some cases closed.
I.E. Exudation in interlobular fissure, and *P.C.* in portal space, owing to which the lobules are much more distinctly outlined than in the normal liver.
l.c. Liver tissue; only change is that capillaries are relatively smaller.

connective tissue nuclei in the portal fissures (stained pink); the capillaries are seen to be somewhat compressed by the columns of swollen liver cells (and by exuded leucocytes).

High power (× 300).—On examining a cell in the portal zone, where the change is always more advanced, note that the cell is distinctly swollen, that it has lost its polygonal form, and is much more rounded

than in the healthy liver cell; that the protoplasm of the cell appears to be exceedingly granular and cloudy looking (probably due to an alteration in the thickness of the rods which make up the intracellular plexus), and the nucleus is somewhat obscured. In some cases the cells appear to be undergoing a process of division or breaking down, and where this is far advanced the whole of the cell may consist simply of a mass of granules, whilst the nucleus has disappeared altogether.

It is probable that, as in the case of the heart, the cloudy swelling is frequently but an early stage of the process known as fatty degeneration.

Fatty Degeneration and Fatty Infiltration of the Liver.

111. Although, for purposes of description, these two conditions are to be taken up separately, it is to be remembered that they merge into one another imperceptibly, and that the same series of causes is probably operating in both cases. Of these causes the more notable are—(1.) An excess of hydrocarbons brought to the liver; (2.) Impaired power of assimilation in the cell itself; (3.) Imperfect oxidation, from whatever cause this may arise.

It is known that, after a meal, the fatty materials brought to the liver by the portal veins collect in the liver cells at the periphery of the lobule, as droplets of fat; very shortly these droplets of fat disappear, as they are gradually burnt off and assimilated. Should the hydrocarbons be supplied faster than the assimilating process goes on, the condition of fatty infiltration of the liver supervenes; whilst, if the protoplasm itself, through loss of vitality or a decreased supply of oxygen, gradually becomes converted into fatty material, what is spoken of as fatty degeneration is the result.

Fatty Infiltration of the Liver.

112. Fatty infiltration, or Adiposis, is found during the physiological process of digestion, and is only a pathological condition where there is an exaggeration of the normal process. It may be due to an excessive supply of fatty matter, maltose, sugar, &c., or to defective assimilation of these; but the essential factor in this

condition appears to be that the fat is derived principally from without, and is not formed from the breaking down of the protoplasm of the cell, though it is accompanied by impaired function of the cell. It is found in patients who have died from phthisis, scrofula, cancer, wasting diseases generally, and, as a rule, is unaccompanied by marked jaundice or ascites. The organ is enlarged, smooth, paler or yellower in colour. The capsule is tense and glistening, and the anterior margin of the liver is considerably thickened and rounded. The tissue pits on pressure, and the indentation remains for some time after the pressure is removed. The lobules, as a rule, are pretty distinctly marked out, each having a pale yellow ring at its periphery, and a brownish red or purple centre : this may be seen even through the capsule. On making a section into the substance of the organ, it is found that the general pallor is distinctly marked, and that the surface of the section has a peculiar yellow mottled appearance ; the tissue is more or less friable. The specific

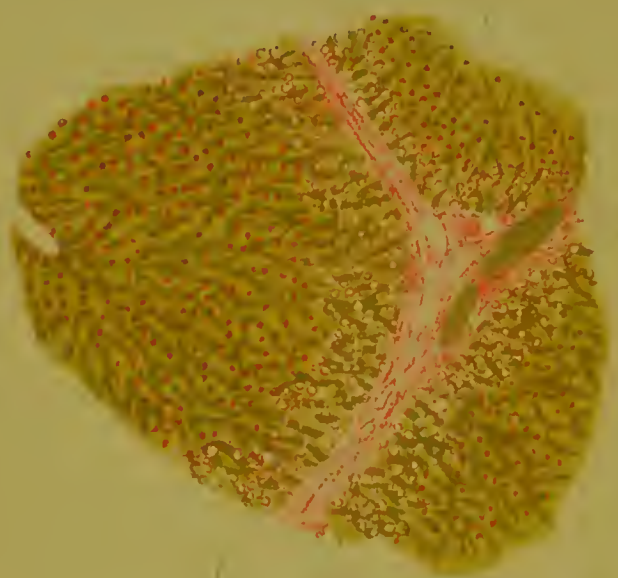


FIG. 11.—Fatty infiltration of the liver—(× 70, after Thierfelder).

c.v. Central or hepatic vein (oblique section).
b.b.b. Bile ducts.
P.V. Branches of the portal vein.
f. Globules of fat infiltrating the liver cells in the peripheral zone of the lobules, bordering on the interlobular space.
n.n. The normal liver cells, occupying the intermediate and central zones of the liver.

gravity may be so much diminished that a piece of the liver will float in water, though the actual weight of the organ may be considerably

increased. When the surface is scraped droplets of oil are collected on the knife. These are readily recognised if the scraping is floated on water. Harden in Müller's fluid (§ 54, p. 43), stain one section in picro-carmine (§ 73, p. 53), one in osmic acid (§ 80, p. 62), and mount these and an unstained specimen in Farrant's solution (§ 98, p. 71).

Microscope, low power (× 50).—Examine a single lobule. The infiltration in the majority of cases is seen to be confined to the peripheral or portal zone, or to that part of the lobule where the blood is emptied from the portal vein into the intercolumnar capillaries. Under this power the droplets of fat appear to be of considerable size, though the size may vary somewhat, as is seen on more careful examination. In the more advanced stages especially, these globules tend to run together, and to form large, clear, strongly refractile droplets, which appear to distend the liver cell completely, and to push the nucleus to one side.

High power (× 300).—The liver cells in the peripheral zone have lost their polygonal form, and are seen to be swollen and rounded.

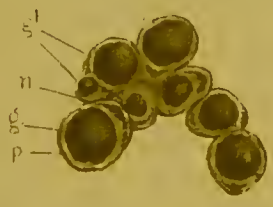


FIG. 12.—Cells from fatty infiltration of the liver. Stained with osmic acid. (× 300.)

p. Thin film of protoplasm, forming, along with the nucleus, *n*., all that is left of the proper substance of the liver cell.

g. A *single large* droplet blackened by osmic acid, and therefore of a fatty nature, contained within the wall of protoplasm. It will be observed that the nucleus is distinctly seen, and is pushed to one angle of the cell, giving rise to the so-called "signet-ring" appearance.

In one cell only are there two droplets of fat, g^1.

The cell is now made up of a thin film or wall of protoplasm, enclosing a single or perhaps two or three droplets of fatty material (stained black by osmic acid). In the picro-carmine stained section observe that one angle of the cell remains, and that in this angle is the nucleus, deeply stained, and very prominent. In consequence of the swelling of the cells, and of their being pressed together, their outlines or boundaries are somewhat indistinct and obscured.

Fatty Degeneration.

113. Fatty degeneration is to be looked for in the liver of patients who die during the course of wasting or exhaustive diseases. It is also constantly met with as a sequel to cloudy swelling, following continued fevers and the exhibition of those poisons already mentioned (§ 110, p. 82), which act by interfering with the proper oxidation of the tissues. It is also seen in Addison's disease, in anæmia, and phthisis, where, in addition to imperfect oxidation, there is decreased vitality of the tissues as a part of a general malnutrition or debility of the system. It is frequently met with in patients who have died of malignant growths, especially cancer.

From the physical characteristics of the tissues, both naked eye and microscopic, the condition is known as the atrophic or wasted form of fatty liver. The organ, in the advanced stage of the process, and where a sufficient number of the cells have become affected, is



Fig. 13.—Drawing of fatty infiltration of the liver (with fatty degeneration at the periphery of the lobule only). Stained with osmic acid. (× 50.)

C. Capsule of the liver.
V.C. Transverse section of central or hepatic vein.
*V.C*¹. Oblique section of central or hepatic vein.
P.C. Portal canal, with various openings. (See Fig. 6.)
P.Z. Peripheral zones of the lobules, in which are the fattily infiltrated and degenerated cells,—the fat globules being stained black by the action of the osmic acid.
G. Small mass of round-celled growth, lying close to the portal space, nearly allied to *tubercle* in structure, but with no giant cell.

markedly wasted, and the weight and specific gravity are diminished, the capsule is somewhat wrinkled, the colour is brown or brownish

yellow, and the tissue appears to be more or less opaque, but pale and friable, and it breaks down readily under the finger.

Harden in Müller's fluid (§ 54, p. 43); prepare for section cutting, (§ 67, p. 48); mount one section unstained in Farrant's solution, (§ 98, p. 71); stain a second section in osmic acid (§ 80, p. 62), and mount in Farrant's solution.

Examine with the low power (× 50). The lobules are distinctly defined, the liver cells are atrophied, and in these atrophied and somewhat angular cells are seen a number of small fat globules, having the dark outline and clear centre. These droplets of fat do not, as a rule, appear to be large, and they give the characteristic black reaction with one-half per cent. solution of perosmic acid. The globules of fat are in greatest number towards the periphery of the lobule; but, in advanced cases, the process extends throughout the lobule. The capillaries are dilated. Between the lobules there is frequently a small amount of exudation readily seen in a picro-carmine stained specimen.

High power (× 300).—Here again the cells are seen to be considerably shrunken, and to have an angular outline. Scattered throughout

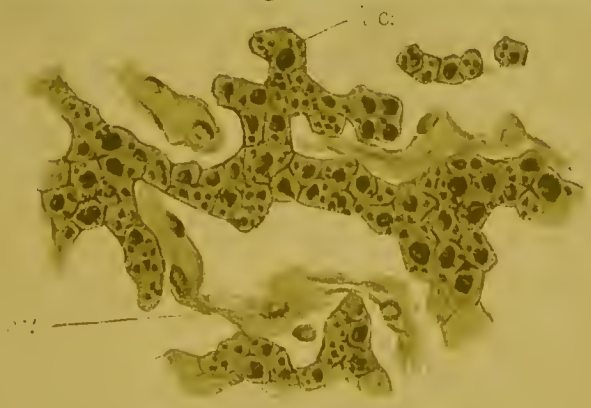


FIG. 14.—Drawing of liver cells undergoing fatty degeneration, taken from near the centre of a lobule. Stained with osmic acid. (× 300.)

l.c. Liver cells arranged in columns. The outlines of these cells are very distinctly marked. The nucleus is not visible in most of the cells, which are small, and have in their protoplasm several droplets of fat,—these droplets varying very much in size, but usually comparatively small.

c.v. Capillary vessels and delicate connective tissue,—the nuclei of both of which are seen slightly stained by the osmic acid.

the protoplasm of the cell are numerous oil globules, never of any great size; for, although some of them may run together, they seldom form

a single large droplet in the centre of the cell. Such of the protoplasm as remains is extremely granular, and the nucleus, when it can be made out, is seen still to occupy its position in the centre of the cell, though, in the majority of cases, it, like the protoplasm, is undergoing division and breaking down. To make out the appearance of the nuclei, stain a section in picro-carmine (§ 73, p. 53), and mount in Farrant's solution (§ 98, p. 71). In consequence of the shrinking of the cells, the outlines of individual cells are readily made out.

114. Where fatty degeneration has been brought on more rapidly, as in the case of phosphorus poisoning, the decrease in size and weight is not so marked, and there are certain other characteristic features, to which special attention must be drawn.

The liver is pale, but at certain points, or it may be almost throughout the whole of the organ, patches of bile-stained tissue and small punctiform hæmorrhages are frequently to be seen. These are due to the rupture of the bile ducts and small arteries, the walls of which have undergone fatty degeneration. In consequence of the bile-staining, the organ is frequently of a canary yellow colour, with hæmorrhagic patches, especially under the capsule. It is not much decreased in size. On examination with the microscope, the protoplasm of the liver cells appears to be almost entirely replaced by fat globules, which in this case are of considerable size; much larger than in the case of ordinary fatty degeneration, as there is no time for absorption of the fat to take place.

Waxy Liver.

115. Synonyms, "Bacony Liver," "Lardaceous" (*Lard*, Fr.), (*Speck Leber*, Ger.), "Waxlike," "Amyloid," "Albuminoid Liver".

Naked eye appearances.—This condition, which is described under the above names, derives them all from some supposed physical characteristics,—its resemblance to smoked ham and so forth. The organ is, in uncomplicated waxy disease, enlarged in all directions. The outline is more square than in the normal liver, and the anterior margin is somewhat thickened and rounded, though not so markedly so as in the fatty liver. The capsule is smooth, glistening, and so tense that the organ does not lie flat on a platter when placed on its anterior

surface, the middle only coming in contact with the platter, the edges being raised. To the touch the substance is firm and hard, like a piece of indiarubber, and is indented with difficulty by pressure of the finger, the indentation disappearing as soon as the pressure is removed.

In advanced cases the fresh section has a peculiar pink colour, somewhat like that of smoked ham or salmon, but the tissue appears to be anæmic. Such a section has a glistening translucent appearance, and looks as if there were a very thin layer of gelatine coating its surface.

On examining a lobule closely, where the disease is not very far advanced, it will be possible to divide it roughly into its three zones: the peripheral or outer zone a pale opaque yellow ring; within this the intermediate zone, which is broader than the peripheral zone, and of the peculiar translucent appearance mentioned above; whilst within this again is a zone which varies somewhat in colour, but usually is a little paler than the normal liver substance. This constitutes the healthiest part of the lobule.

Now pour a watery solution of iodine, about the colour of dark sherry (§ 77, p. 61), over the fresh surface, and there is at once seen a selective staining. The translucent ring is stained a deep mahogany, red or brown colour, the other zones taking on a canary yellow staining. This translucent or mahogany brown area is the portion of the lobule in which the lardaceous material is deposited. Harden in spirit (§ 52, p. 42), and make sections (§ 61, p. 48, *et seq.*).

Low power (× 50).—Place a thin section of the tissue on a slide, and examine without a cover glass. It will at once be observed that in the intermediate zone there is a series of columns of somewhat compressed liver cells, whilst between these are irregular, translucent, homogeneous looking streaks. These streaks, as will be found later, are the capillary vessels, in the walls of which certain changes have taken place. The cells in the central zone appear to be more or less healthy, whilst those in the peripheral zone are either healthy or are undergoing fatty infiltration. Allow a drop or two of the watery solution of iodine to run over the specimen from one margin, and examine the section by transmitted light, when the liver cells will appear to be stained a dark yellow or

brownish yellow colour, whilst the fatty globules and liver cells in the peripheral zone are stained a canary yellow, and the homogeneous

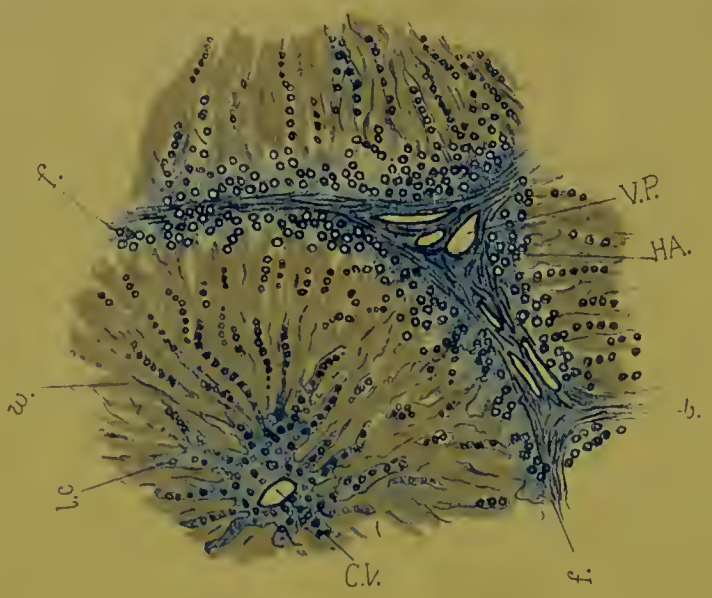


FIG. 15.—Section of "waxy" liver, with some fatty infiltration of the peripheral zone—(× 70, after Thierfelder).

w. Capillaries of intermediate zone, which have undergone the waxy change. Stained red violet.
H.A. Small branch of the hepatic artery, similarly stained; also stained red violet (middle coat).
C.V. Central vein.
V.P. Branch of portal vein, and (*b*) small bile duct in interlobular space.
f. Liver cells of peripheral zone, in which is fatty infiltration.
l.c. Liver cells, angular; atrophied and degenerating, but stained blue like the other tissues; unaffected by the waxy change.

streaks are stained a little deeper yellow. Whilst examining, suddenly turn off the light from below the stage, when the parts which, before, were of the intermediate yellow, now appear to be of the dark brown colour similar to that observed with the naked eye, and the liver cells previously dark now appear to be yellow. This specimen must be mounted in the iodine mounting fluid (§ 77, p. 61), and ringed with Canada balsam or zinc white cement without delay, as, unless this be done, the free iodine evaporates at the margin of the cover glass, and the characteristic staining disappears. This specimen should be kept for examination under the high power (× 300), and for comparison with a section stained as follows:—

Allow a section to stain for about ten minutes in a watery solution of methylaniline violet or Dresden Telegraphen Tinte (of

such strength as will readily allow the light to pass through it when in a three-quarter inch test tube). Wash well in water, mount in Farrant's solution, and examine under a low power (× 50). The homogeneous material has taken on a beautiful

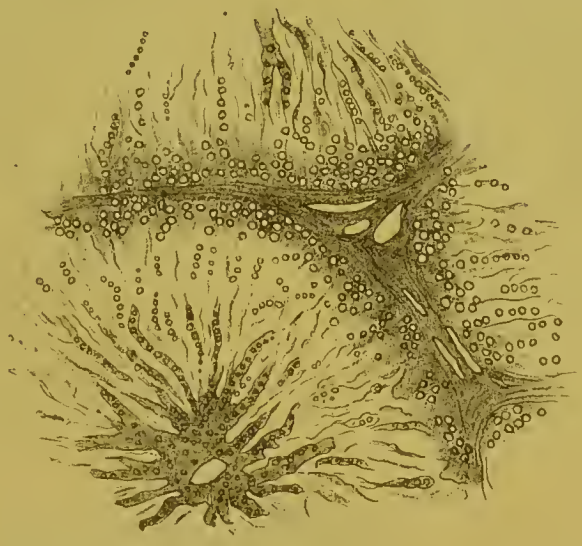


FIG. 16.—Waxy liver, unstained. (See Fig. 15.)

rose pink or red violet colour, whilst the other tissues are coloured slaty blue. This rose pink is highly characteristic of the waxy degeneration, and picks out most accurately and minutely the diseased tissues. Examine first the portal spaces, and observe that

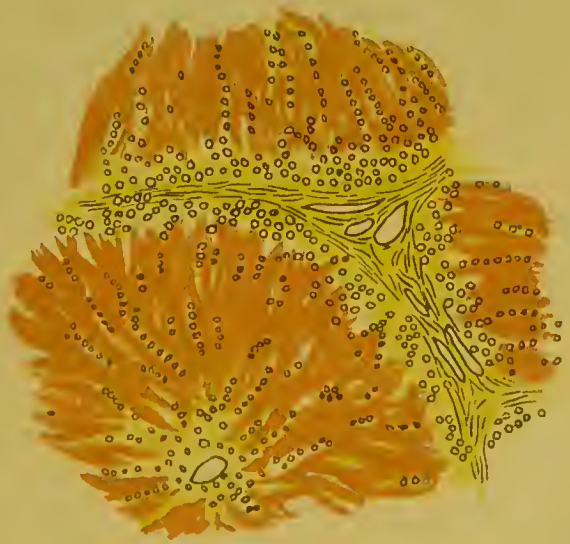


FIG. 17.—Stained with iodine and examined by reflected light. (See Fig. 15.)

the small arterioles of the hepatic artery are stained rose pink—this coloration being confined more especially to the middle coat of the vessel. In the intermediate zone, where the change is most advanced, the cells become more angular, are attenuated looking, and even with this power may be observed to be granular and atrophied; but there is seldom or never pink reaction within these cells.

(× 300.)—The arteriole in the portal canal is affected as follows :—The middle coat is picked out, as it were, and if a longitudinal section is seen, certain areas or bands of this are further selected. Later the inner coat becomes more or less involved, but only in its deeper layers, as the endothelial cells lining the vessel have become granular and fatty looking, but still give the blue reaction.

Under this magnifying power the capillaries in the intermediate zone are observed to be the special seat of the affection. The walls are enormously thickened, and the lumen of the capillary tube in

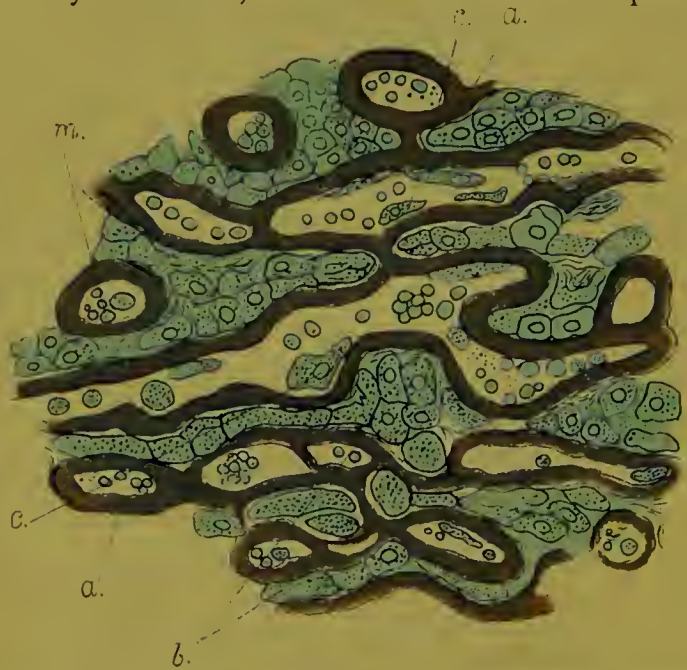


FIG. 18.—Waxy liver, stained with methylanilinc violet and mounted in glycerine—(× 350, after Cornil).

a.a. Capillary walls thickened and waxily degenerated, stained red violet.

c. Endothelial cells, and

m. Coloured and colourless blood corpuscles, normal, and stained a slaty blue colour.

b. Hepatic cells between the capillaries are also normal, and stained the same blue colour.

many cases appears to be altogether obliterated, so that little is to be seen but thick bands of the translucent homogeneous material, stained

a beautiful rose pink colour, between which lie bands or rows of liver cells. These cells are seen as under the low power, atrophied, angular, and are in many cases undergoing fatty degeneration; the nucleus is in its normal position, but is somewhat obscured, and the outline of the cell is distinctly marked; there is seldom, however, any pink reaction to be seen in any part of the cell, even under this power.

The capillary vessels in this position are to be considered as made up of three coats; a single layer of endothelial cells in immediate contact with the blood current; outside this is a thin membraneous structure, composed of connective tissue fibrils, or possibly of an elastic tissue; and external to this again are connective tissue cells, the processes of which are continuous with the basement membrane. These are spoken of as perithelium. According to the latest researches the waxy change takes place in the basement membrane between the two layers of cells, or in the connective tissue filaments between these layers. The delicate filaments become enormously swollen, and ultimately become so prominent as to overshadow the other structures. The endothelial cells become granular and fatty. In consequence of this enormous thickening of the walls of the capillary vessels two results ensue—one from the extension inwards,—gradual narrowing, and ultimately complete obliteration of the lumen of the vessel;—and the second from the extension outwards—the compression of the columns of liver cells, leading to atrophy and molecular disintegration of the proper substance of the liver.

On examining (× 300) the iodine stained section it will be noticed that in the liver cells are a few granules which take on the same staining as does the waxy material; for which, however, they must not be mistaken, as it is found that glycogen, when separated, gives the same reaction with iodine, but not with methylaniline violet, by which reagent the two substances may be distinguished from one another.

A third method of staining is to dip the section into a weak solution of iodine, and then convey it to a 2 % solution of sulphuric acid. This is Virchow's original method. He described the reaction as blue with the lardaceous material, whilst the other tissues give a yellow colour. The other methods, however, are more certain and more convenient, though it will be as well to try this method in making investigations on the subject.

This condition of the liver is to be looked for in all cases—(1.) where there has been long-continued suppuration, especially of bones; (2.) in cases of chronic phthisis, where the discharge from the cavities formed has been going on for some time; (3.) in cases of syphilis, congenital or acquired.

From these facts it may be readily understood how it is that the condition is found complicated with fatty infiltration in the peripheral zone, or fatty degeneration, tubercle of the liver, cirrhosis and syphilitic scars. All these conditions modify the typical waxy form of the liver to a greater or less extent where they are present, and this fact must always be borne in mind when an examination of a waxy liver is made.

"Nutmeg" or "Cardiac" Liver ("Cyanotic" Atrophy, Chronic Venous Congestion of the Liver, &c.)

116. Nutmeg liver is met with especially in cases where there has been cardiac disease, or extensive lung disease, such as emphysema, chronic phthisis (fibroid), and so on; in fact, in any condition where there has been an obstruction to the return of the blood by the inferior vena cava to the thoracic cavity. Where the primary lesion is in the heart, say at the mitral valve, a corresponding condition is found in the lungs, in the kidney, spleen, intestines, and in the portal system generally, so that amongst other symptoms during life are diarrhœa, hæmorrhoids, chronic intestinal catarrh, varices, and ascites. The effects are to a very great extent mechanical, and are due to an increased pressure in the hepatic vein, this pressure manifesting itself by its effects first in the central or intralobular veins, and later in the sublobular veins and intermediate and peripheral parts of the portal capillary veins.

In the early stages the organ is somewhat enlarged, the capsule tense, thin, and translucent: later, the liver appears to be atrophied and tough, but still contains a considerable quantity of blood, which gives the section a very dark red colour; at this stage, too, the capsule may be thickened in patches, or may have on its surface (especially where ascites has been present) small villous growths,—papillomatous growths, as they are sometimes incorrectly named. The openings of the hepatic veins are patent, and from this fact appear to be more numerous.

Examine a lobule, and observe that it can be divided into three zones, each of which may be seen more or less distinctly. The central is deep red in colour, and is engorged with blood; external to this is the brownish yellow intermediate zone, the yellow tinge here being due to bile-staining, whilst the peripheral zone is pale and fatty looking. From this peculiar coloration the name "nutmeg" liver is derived, and as the name refers simply to the appearance of the tissue it is perhaps as good a one as can be used.

To preserve the organ for examination, pieces of it should be hardened in Müller's fluid (§ 54, p. 43). The tissues are then soaked in water, gum, and syrup, and sections made (§ 67, p. 48). Mount one section unstained in Farrant's solution (§ 98, p. 71), stain a second section in picro-carmine (§ 73, p. 53), and mount in Farrant's solution.

Examined under a low power (× 50), the central or hepatic vein is seen to be considerably dilated, so that the lobules are much more readily made out than in the normal liver.

The capillaries leading to this central opening are also considerably dilated, and are frequently filled with blood. Between the dilated capillaries the liver cells are becoming atrophied, angular, compressed, and granular looking, whilst in the immediate neighbourhood of the central vein they contain masses of brown or orange red granular pigment, derived either from the blood, or more probably from the liver cells themselves.

High power (× 300).—The walls of the dilated vein and its surrounding capillaries are now seen to be considerably thickened, in some cases forming distinct fibrous bands and circles. The pigment in the cells situated in the inner part of the lobule is seen much more distinctly in the periplast of the cells, not obscuring the nucleus, unless the cell is entirely filled with the colouring matter. The shrinking and atrophy of the liver cells is more clearly made out, and in some cases small fat globules are seen lying scattered throughout the angular mass of protoplasm which represents the cell.

The atrophy of the liver cells is due to the pressure of the blood distending the capillaries, so that the columns of liver cells between adjacent vessels are compressed, as these vessels become swollen, varicose, and tortuous. In the later stages of the disease, the liver

cells may have disappeared entirely from the immediate neighbourhood of the central vein, and there is left simply a cavernous structure, made up of the fused walls of capillary vessels, forming bands of fibrous tissue, between which are spaces filled with blood.

In certain cases bands of fibrous tissue continuous with these central fibrous vascular walls run to the periphery, and so cut up the lobule into several segments. Along with this there is frequently an

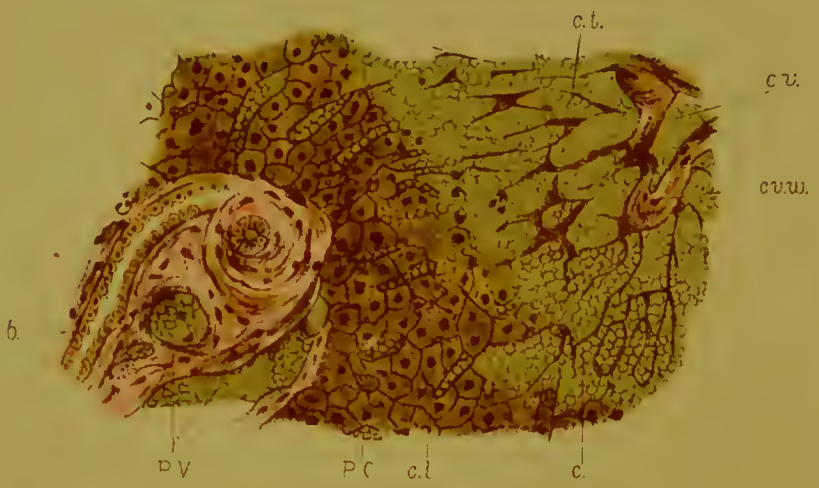


FIG. 19.—Section of "Nutmeg" liver—advanced (× 300, slightly reduced, after Thierfelder).

c.v. Dilated central vein, the wall of which (*c.v.w.*) is thickened and fibrous looking, with here and there some golden yellow pigment scattered in its substance.
c.c. Capillaries in the central zone, greatly dilated and filled with blood, with (*c.t.*) thickened walls similar in appearance to the thickened walls of the central vein.
l.c. Liver cells of peripheral zone.
P.C. Capillaries in peripheral zone, not greatly distended.
P.V. Branches of the portal vein distended with blood.
b. Bile ducts, lined with more or less cubical nucleated epithelium.

increase in the amount of connective tissue in the interlobular spaces and fissures. This is a form of cirrhosis peculiar to the nutmeg liver, and frequently occurs during the course of the disease in its later stages.

In the peripheral zone, pretty well marked fatty infiltration is often met with, the presence of which is probably accounted for by the slower passage of the blood through the portal system, in consequence of the obstruction to the outlet of blood from the hepatic system.

In consequence of the obstruction to the outlet of the blood from the vena cava, the hepatic vein cannot empty its contents so readily, and in turn the obstruction is felt in the sublobular, the central or

intralobular veins, the intercellular capillaries, and lastly, in the portal vessels; there is a partial stasis of the blood. In addition to this the liver cells are somewhat compressed, and hampered by the increased pressure from the dilated capillary vessels, and their nutritive activity is impaired; hence the fatty infiltration.

Common Cirrhosis of the Liver.

117. Synonyms, "Gin-drinker's" Liver, "Hobnail" Liver, "Polylobular Cirrhosis," "Alcoholic Cirrhosis," "Granular" Liver.

In this condition the liver is, especially in the later stages, considerably decreased in size. The organ is anæmic, firm to the touch, almost hard, and the feeling of it may be compared to that of a piece of

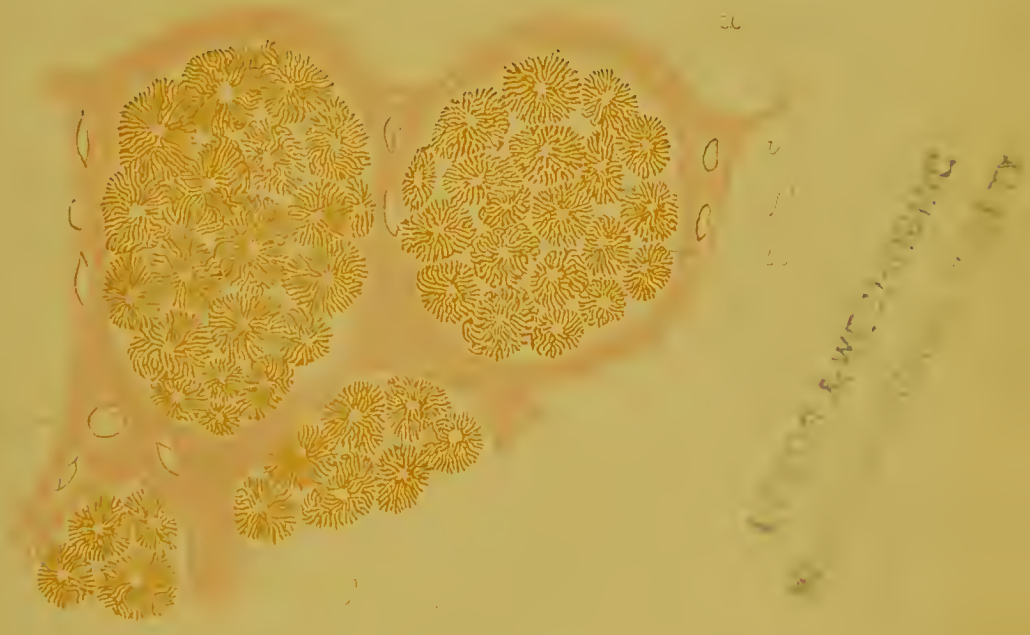


Fig. 20.—Diagramatic sketch of common cirrhosis of liver.

c.t. Thickened capsule, from which bands of fibrous tissue (*f.t.*) run along the lines of the medium sized portal veins (*P.V.*).

v. Small vessels supplying this tissue with blood from the hepatic artery.

l.c. Mass of a considerable number of lobules enclosed by the bands of tissue.

l.c^1. A smaller mass.

soaked leather. On the surface are a number of small projections about the size of the head of a hobnail or "tacket," and between

these are depressions or fossæ. The deeper layer of the capsule—Glisson's capsule proper—is more or less thickened and opaque looking. On making a section, the tissue is felt to be firm and tough, and on examination greyish red gelatinous looking bands of fibrous tissue are to be seen running in various directions throughout the substance of the organ, and cutting it up into a series of areas of parenchymatous cells. These areas are of various sizes, generally from one-sixth to a quarter of an inch in diameter (a lobule being from one-sixteenth to one-twentieth of an inch in diameter). They are of a tawny yellow colour, and have a bile-stained look. As a rule, the cells of several lobules are contained within each of the fibrous capsules, from which they may be turned out *en masse*.

These fibrous bands are seen to be continuous with the deeper thickened layer of the capsule, into which they run at the point of depression around the hobnail elevation. This elevation, consisting apparently of a yellowish brown mass of cells, compressed by the contracting fibrous bands, is pushed in the direction of least resistance, *i.e.* to the surface.

Harden a piece of this liver in Müller's fluid (§ 53, p. 42), and a second piece in spirit (§ 52, p. 42), cut (§ 67, p. 48), stain a section, on one margin of which must be a piece of the capsule, in picro-carmine (§ 73, p. 53), and mount in Farrant's solution.

Low power (× 20).—At the margin of the section the thickening of the capsule is seen as a mass of pink fibrous tissue, from which bands of different sizes may be observed running down into the liver substance from the lowest parts of the sulci. Between these fibrous bands are masses of six, eight, or ten lobules, corresponding in position to the elevations above mentioned.

The fibrous bands split up, and are continuous in the substance of the liver, with other bands greatly thickened running along with the *medium sized* branches of the *portal vein*, some of which appear to be more or less diminished in size by the pressure of the newly formed tissue around them. It is somewhat difficult to make out the individual lobules, as there is, especially in the earlier stages of the disease, no increase in the amount of interlobular tissue, whilst, owing to the pressure exerted by the contracting fibrous bands in the larger portal spaces, the lobules are pressed together and the central vein is more or less closed.

High power (× 300).—It will be well to stain a thin section with logwood (§ 74, p. 57), mount in Canada balsam (§ 96, p. 69), and then examine the two sections together. Examining first the newly formed

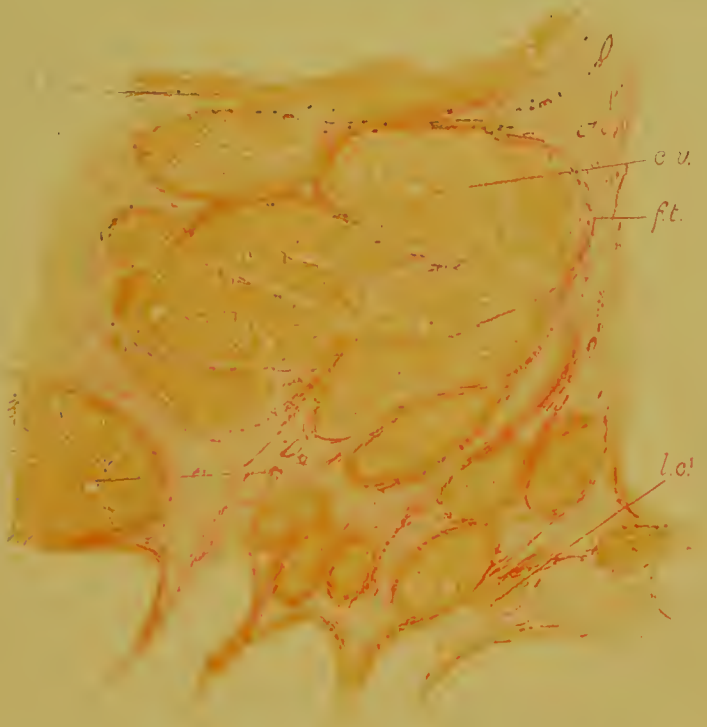


FIG. 21.—Drawing of a section of common cirrhosis of the liver, stained with picro-carmine. (× 20.)

f.t. Bands of newly formed fibrous tissue running into the substance of the liver, and cutting it up into masses of cells of various sizes.
l.c. Containing a number of lobules.
*l.c*¹. Containing part of a lobule only, with here and there masses, of intermediate sizes.
c.v. Central vein of a lobule.
v. One of the newly formed vessels, supplying the fibrous tissue of the blood from the hepatic artery.

bands of fibrous tissue, it is found that in the early stages especially there are enormous numbers of rounded nuclei, each surrounded by a small envelope of protoplasm. Amongst these are other cells of larger size, which are apparently derived from the proliferating connective tissue corpuscles. In the later stages it may be observed that the number of round nuclei is apparently much diminished, whilst in place of them appear (according to the method of staining) pink or delicate blue bands of fibrillated tissue; and scattered at intervals through this are numerous elongated nuclei, which are the nuclei of flattened connective

tissue corpuscles, around which a fibrillated periplast has been formed. The more advanced the disease, and the more contracted the organ, the more fibrous does this fibro-cellular tissue become, until in some parts it may be represented by only a band of contracting cicatricial tissue. This fibrous tissue in all cases, however, is found to be exceedingly vascular, and by injection it may be proved that

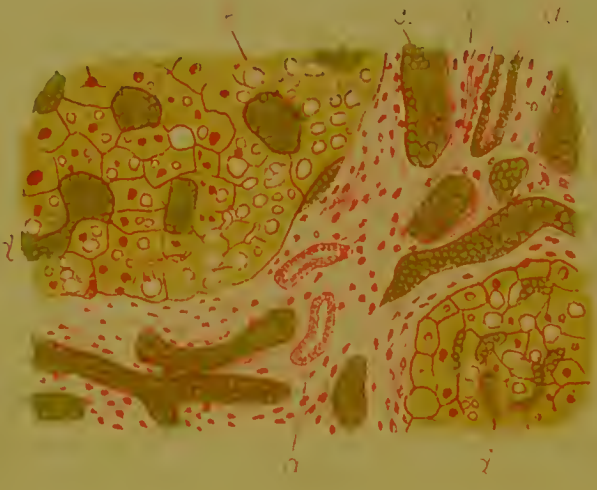


FIG. 22.—Section of common cirrhotic liver (after Thierfelder), (× 300 slightly reduced), in which are two masses of liver cells, between which is a band of fibrous tissue running in the portal space.

a.a. Small bile ducts lined by epithelial layer.
b. Nuclei of connective tissue corpuscles.
c. Newly formed blood-vessels, supplied by the smaller branches of the hepatic artery.
d. Sections of intercolumnar or portal capillaries filled with blood.
e. Globules of fat in the compressed and fattily degenerating liver cells.

this vascularity is due to the formation of new capillaries and small vessels, which derive their blood supply from the pre-existing small branches of the hepatic artery. These new vessels, embryonic in character, often consisting of mere channels lined by a single layer of endothelial or flattened connective tissue cells, are frequently found to be filled with blood, especially if the tissue has been preserved in Müller's fluid. Hence, if a fresh "nutmeg" liver is injected with a fine injecting fluid, it becomes deeply coloured—carmine, say—and the colouring is especially well marked along the course of the bands of fibrous tissue.

The bile ducts appear to be unaltered in number or size, though relatively their number appears to be greater. They are seen, in longitudinal section, as double rows of nuclei in the logwood-stained specimen ; but in the picro-carmine stained specimen the epithelium

lining these smaller ducts may be readily made out, especially in transverse sections of the ducts (Fig. 20).

On examination of the masses of cells, it is observed that they are at all points somewhat closely pressed together, and that sometimes they contain globules of fat (Fig. 20).

At the periphery of these masses of lobules, thin bands of the fibrous tissue may be seen shaving off layer after layer of liver cells,

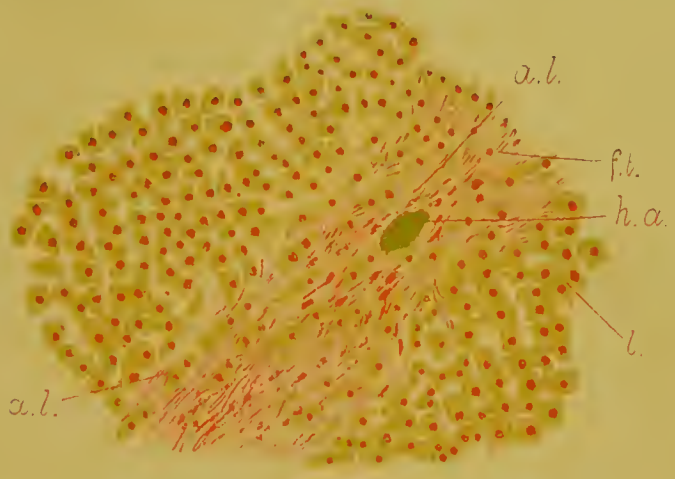


FIG. 23.—Drawing from a section of common cirrhosis of the liver, stained with picro-carmine. (× 300.)

l. Healthy liver cells near the centre of the mass. At the periphery of the masses of cells are numbers of atrophied liver cells (*a.l.*) sliced off by the new fibrous tissue (*f.t.*) growing in this position.

h.a. Section of a small branch of one of the newly formed vessels, bringing blood from the branches of the hepatic artery to the growing fibrous tissue.

in this way gradually cutting down the size of the masses. The cells so cut off are compressed between the layers of fibrous tissue, lose their nuclei, and become flattened and angular, whilst the protoplasm of the cell becomes granular, and sometimes contains droplets of fat or pigment and granules, Eventually these cells disappear altogether. This cutting off of layers of cells is very characteristic of the poly-lobular form of cirrhosis.

To sum up. The change consists essentially in an increased growth of fibrous tissue in Glisson's capsule, and in the prolongations from it, which run along with the larger or medium sized branches of the portal vein. These branches of the portal vein become constricted

by the surrounding growth of tissue, and the larger branches of the portal system become dilated. As a result of this, considerable dropsical effusion may occur. This continues, unless or until an anastomotic venous circulation is set up through the veins in the suspensory ligament and umbilical cord, or through new vessels in the adherent capsule. Along with these changes in the portal circulation there is increased pressure in the hepatic artery, which then sends branches to the newly formed fibrous tissue, and also partially takes on the function of the portal vein.

The biliary passages are, as a rule, unaffected in this condition, consequently jaundice very seldom appears during the course of this disease. The lobules are pressed together, and their outlines lost. The liver cells undergo the changes mentioned above.

There is a less common form of alcoholic liver, in which the organ is greatly enlarged; the naked eye appearances are much like those in the following, or biliary, form; but we find that the distribution of the connective tissue is not so regular, the liver parenchyma is cut up into masses of very various sizes, and in the cells very marked fatty degeneration and infiltration take place. The splitting off of cells from the periphery of the masses points to the fact that there is here a rapidly advancing condition similar to the above, but more advanced, though the biliary form of cirrhosis is sometimes simulated, and the connective tissue runs into the substance of the lobules with the formation of new bile ducts, as in that form.

"Biliary" Cirrhosis.

118. Synonyms, "Hypertrophic" Cirrhosis, "Monolobular" Cirrhosis, "Fine" Cirrhosis, &c.

In this form of cirrhosis the organ is, as a rule, increased in size, and in some cases is considerably larger than normal, the capsule is smooth, but very finely granular, feeling like a piece of morocco leather, and the substance of the liver is hard and frequently brittle. On section the tissue may be of various colours, from yellow or reddish yellow to a bright or even a dark green, as the whole of the tissues may be considerably jaundiced, or bile-stained. It is here extremely difficult to make out where the fibrous tissue ends and the

liver substance begins, as the gelatinous looking fibrous tissue in this form passes round and encloses individual lobules. The portal veins may in some cases appear to be distended, but this is by no means an invariable condition. Harden a piece of the organ in Müller's fluid (§ 53, p. 42), and a second in spirit (§ 52, p. 42); stain a section in picro-carmine (§ 73, p. 53), mount in Farrant's solution (§ 98, p. 71), and one in logwood (§ 74, p. 57), and mount in Canada balsam (§ 96, p. 69).

Low power (× 50).—The capsule does not appear to be particularly thickened, but if the small portal or interlobular spaces and the interlobular fissures are examined, it will be observed that there is a considerable increase in the amount of new tissue, either in a cellular or fibro-cellular form.

It is in fact an interlobular or monolobular cirrhosis. In the newly formed tissue are frequently seen a number of double rows of nuclei, which are recognised as the nuclei of the epithelial cells of the small bile ducts. These bile ducts are evidently much increased in number, and where the disease is advanced they are seen to run along with fibrous tissue into the substance of the lobule. The fibrous bands, running at right angles to the periphery of the lobule, may encroach from all sides, and split up the lobule into small masses of cells, which gradually become atrophied, and finally may disappear.

High power (× 300).—The connective tissue is seen to resemble that in the common form of cirrhosis, but here it appears to be formed in connection with the walls of the smaller bile ducts instead of around the branches of the portal vein. The larger branches of the bile ducts are constricted by the growing and contracting tissue, in consequence of which there is increased pressure in the smaller branches, which appear to be somewhat distended. They are also seen to be much more numerous, especially at those points where the connective tissue is invading the lobule from its margin. Near the advancing connective tissue, and in the course of these newly formed bile ducts, the liver cells appear to be undergoing atrophic changes, the nuclei are dividing, and the liver cells are splitting and becoming flattened.

Before continuing the consideration of this condition, it will be well to see what is the structure of the bile ducts, commencing at the larger branches and passing backwards.

The largest bile ducts are lined by a layer of distinctly columnar cells, external to which is a limiting membrane, probably made up of endothelial cells; outside this again is a layer of non-striped muscular fibre. The lumen of these tubes is comparatively large, and after death their walls are thrown into folds by the contracting muscular fibre. The smaller bile ducts have a comparatively thick

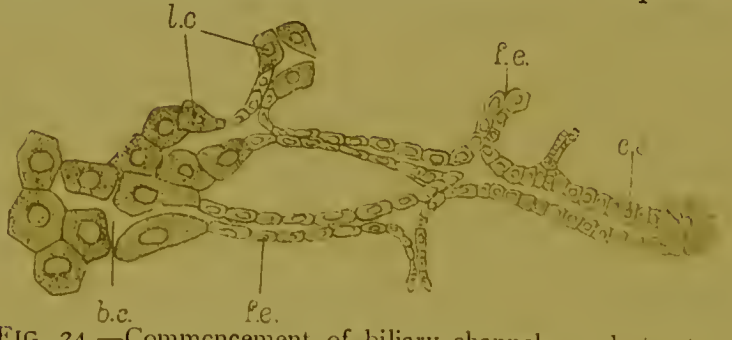


FIG. 24.—Commencement of biliary channels, and structure of smaller bile ducts (after Klein and Noble Smith).

b.c. Biliary canaliculi in the angles between adjacent liver cells.

l.c. Liver cells, slightly modified, just before the commencement of the bile duct proper with its lining of flattened epithelium (*f.e.*), (intermediary portion of the duct).

c.c. Cubical epithelium of the somewhat larger bile duct.

wall and small lumen; the epithelial cells are not so distinctly columnar, and there is now no muscular coat. At or in the margin of the lobule the small ducts are much branched; the epithelial cells form a single flattened layer, but there is still a distinct *membrana propria*. This, the intermediary portion of the duct, opens directly and suddenly into the bile capillaries, which consist simply of channels formed by the apposition of the grooved surfaces of several liver cells. Thus, a bile capillary is generally placed at the angle between three or four liver cells, a groove or depression in each cell forming part only of the capillary channel; though more minute channels still probably run in the substance of the liver cell. When the structure of these bile ducts is thoroughly grasped, it is naturally much easier to understand the mode of formation of the new bile ducts. In the coarse new connective tissue formation, as it penetrates the periphery of the lobule, the liver cells are seen divided and flattened, and quite close to and continuous with them are the small bile ducts running for some distance into the lobule, so that it may be safely concluded that the new bile ducts are formed from the splitting up of these liver cells—a process of division of the nucleus

and then of the cell—followed by further subdivisions, until, in place of the three or four cells surrounding the bile capillary, there are

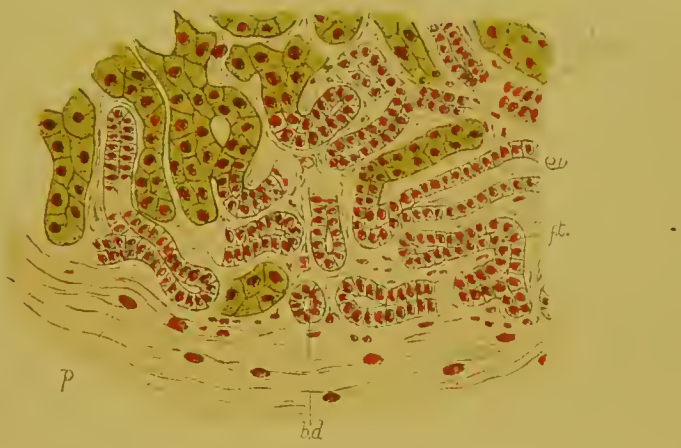


FIG. 25.—Drawing (after C. Sabourin) (× about 300) in which is shown the gradual ingrowth of fibrous tissue (*f.t.*) from the portal space (*P.*) into the substance of a lobule. Where this is taking place, whether as cause or effect, the liver cells (*l.c.*) are becoming modified (*e.b.*) and present very much the appearance of the slightly columnar or cubical cells found lining the smaller bile ducts in the normal position (*b.d.*)

numerous small flattened cells resembling those around the smaller bile ducts;—the process consists, in fact, of a reversion of the liver cell to its embryonic or epithelial type.

The condition throughout is due in all probability to an inflammatory change set up around the branches of the bile duct, either by some chemical irritation, or by irritation caused by some obstruction to the outflow of the bile from the ducts.

In certain cases monolobular cirrhosis may be set up by a periphlebitis, but this form is much less common, and appears to be unaccompanied by any new formation of bile ducts.

From the above short descriptions of the two forms of cirrhosis, the following differences will be at once observed to exist between them :—

IN COMMON CIRRHOSIS.	IN BILIARY CIRRHOSIS.
1. The bile ducts are but little involved in the growth of connective tissue, there is little or no jaundice or bile staining of the liver tissues, and no new bile ducts are found on microscopic examination.	1. The bile ducts are the first structures involved, the jaundice and bile staining of the liver substance is, as a rule, well marked, and there is a new formation of bile ducts.

2. In consequence of the new growth of tissue taking place along the course of the portal veins, especially the medium sized branches, ascites is a very common complication in this form, as are also hæmorrhoids, varicose condition of the veins of the œsophagus, congestion, or even hæmorrhage in the gastro-intestinal tract.	2. The portal veins are not involved in the change, and ascites and the rest are rare.
3. In the early stages, in consequence of the increased amount of young connective tissue in the portal spaces, there is considerable enlargement of the organ; but in the later stages, where this tissue is becoming fibrous and cicatricial, and is contracting, there is, as a rule, a considerable decrease in the size of the liver.	3. In consequence of the large amount of new tissue diffused throughout the organ, it is considerably increased in size.
4. The liver is rough, with projections about the size of a hobnail on its surface. The capsule is thickened and opaque, especially at the bottom of the fossæ which surround these projections.	4. Surface is smooth (morocco leather feeling), and the capsule is not thickened.
5. The masses of liver cells vary very much in size, some consisting of several lobules, whilst others are smaller than a lobule. Each of these masses forms a distinct area, having a rounded outline surrounded by a fibrous zone, and from the fibrous capsule the mass of liver cells can be easily turned out.	5. The masses of liver cells consist of single lobules, which are, however, considerably diminished in size, and the cut surface has a more or less uniform and finely granulated appearance.
6. On microscopic examination, it is seen that the process is going on chiefly at the periphery of the lobules, but that groups of lobules are affected.	6. The single lobules above mentioned are surrounded by bands of fibrous tissue, which bands, however, are not confined to the periphery, but "invade the substance of the lobules."

Syphilitic Cirrhosis (Congenital).

119. This condition is met with in the livers of children who are still-born, or who die shortly after birth, and who come into the world with all the marks of syphilis upon them. The whole organ is enlarged, the tissue is firm, tough, and pale, the pallor being more marked at certain points, whilst on the surface of the liver there are frequently purplish nodular projections. The pale parts are

those in which the diseased condition is most advanced. In the centre, these masses present a pearly white appearance. Surrounding the centre is a yellow and then a more vascular zone. These pale nodules are about half an inch in diameter. If the disease be very far advanced, the lobules are almost entirely obliterated, and there is no definite structure left, the parenchyma appears yellow, mottled with reddish or greyish brown, and delicate looking striæ run through it irregularly. It is to be remembered that in the earlier stages of the disease the structure of the liver to the naked eye appears to be little altered, even when grave microscopic changes have occurred. The only evidences of a diseased condition are then the increased weight and firmness of the organ.

A piece of this liver should be hardened in alcohol (§ 51, p. 42), and a second in Müller's fluid (§ 53, p. 42). To stain sections satisfactorily, add half a drachm of ammoniacal carmine solution, and a similar quantity of methylaniline violet, to one and a half ounces of water. Allow the sections to stand in this solution for several hours, and then wash in water, and mount in Farrant's solution (§ 98, p. 71), or keep in preservative fluid (§ 71, p. 52).

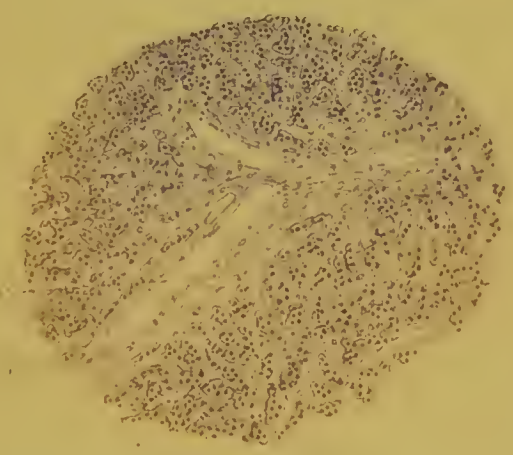


FIG. 26.—Drawing from a section of syphilitic cirrhotic liver, stained with carmine and methylaniline violet. (× 55.)

P.S. Increase of fibrous tissue in portal spaces. This increase of fibrous tissue is seen to extend from this position for some considerable distance into the lobules, the columns of liver cells (*l.c.*) are seen to be much more atrophied at the margin than at the centre of the lobule (*l.c*^{1}).

c.t. Nucleated fibrillated tissue between the atrophied liver cells.

Low power (× 50).—Near the portal spaces in which is an increase in the amount of fibrous tissue there may be seen, apparently con-

tinuous with the perilobular tissue, a quantity of clear looking material with numerous rounded nuclei. Between the clear bands are small linear or Y-shaped masses stained deep purple; these deeply stained masses are separated from one another by spaces, two or three or even more times their own diameter. The wider the spaces the smaller are the dark coloured masses. Further away from the portal spaces the tissue becomes more and more like that seen in a normal liver, until at certain points the structure is perfectly normal.

High power (× 300).—The deeply stained masses are now seen to be rows of liver cells which are undergoing more or less marked changes. Where the lines are comparatively broad, the structure of the liver cell is as yet little altered; there is simply a slight compression of the cell. Where the lines are narrow, the cells are seen to have undergone more extensive changes. They are now angular, shrunken, and granular looking, and are evidently undergoing atrophic degeneration; the nuclei are somewhat obscured, or in certain cases are altogether lost. The substance between these bands of atrophied

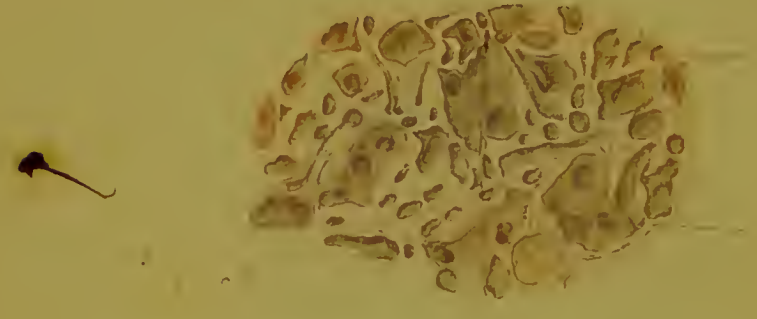


FIG. 27.—Drawing from a section of syphilitic cirrhotic liver, stained with carmine and methylaniline violet. (× 440.)

l.c. Small masses of granular and somewhat atrophied liver cells, between which is the increased amount of nucleated and fibrillated connective tissue (*c.t.*)

liver cells is composed of a nucleated connective tissue. Around the connective tissue cells, and formed by them, is a delicate fibrillated periplast, which forms the transparent tissue, as seen under the low power. The increased size of the organ is due to the vast increase in the amount of the intralobular connective tissue. In order to understand the nature of this change, it must be remembered that communicating with the interlobular lymphatics at the margins of the lobules are "minute spaces extending between the liver cells and the capillary

blood-vessels, and containing numerous branched connective tissue corpuscles." Subsequently the capillary vessels are lined by a layer of endothelial cells, which, like the connective tissue corpuscles, are of mesoblastic origin. The change consists essentially in a proliferation (*a*) of the endothelial lining of the capillary vessel, and (*b*) of the connective tissue corpuscles or endothelial cells, which may be said to line the lymph spaces between the capillaries and the liver cells. Around these proliferated cells the fibrillated periplast is formed; there follow the gradual compression and atrophy of the proper parenchyma of the organ, with a continually increasing space between the columns, which are cut up into short detached masses of angular, atrophied liver cells, of granular appearance.

Syphilitic Gumma of the Liver.

120. The syphilitic gumma is closely related to the above form of cirrhosis, and is generally seen in the caseous stage; but it is to be remembered that this caseation is a degenerative process taking place in the gumma. It is one of the forms of syphilitic lesion found in the livers of adults, but then only in this caseous form. To find a growing gumma in this organ it is necessary to examine the liver of a syphilitic child, where gummata are frequently found in connection with the syphilitic form of cirrhosis. Such a growing gumma is a tumour, varying greatly in size (from that of a pea to that of a marble, or even larger), of a rosy-grey colour, when seen on section, and *containing vessels;* it gradually merges into the surrounding tissues, with which it is intimately connected. The surrounding tissue is made up of very vascular fibrous bands. On the surface of the liver are irregular patches, deep red in colour (redder than the rest of the liver substance), varying from the size of a pea to that of an apple.

The caseous gumma is usually found in the adult, situated near the surface of the liver, enveloped in a fibrous capsule. It most frequently occurs on the upper surface of the organ, and is found especially near the suspensory ligament. In consequence of the contraction of the fibrous capsule surrounding the mass, there is a distinct depression at the periphery; it appears to be situated in fibrous cicatrices, near the surface of the liver. Harden a

piece of the organ in alcohol (§ 51, p. 42); and a few pieces in Müller's fluid (§ 53, p. 42); stain one section in picro-carmine (§ 73, p. 53); and mount in Farrant's solution (§ 98, p. 71); a second section in logwood (§ 74, p. 57); and mount in Canada balsam, (§ 96, p. 69); then treat a third as in syphilitic cirrhosis (§ 119, p. 117).

Low power (× 50).—On examining a section taken from the liver of a syphilitic child, in which is one of these nodules, the first point noticed is that the growth is situated in newly formed intralobular fibrous tissue; in other words, that the formation of a gumma is preceded by a syphilitic cirrhosis identical with that already described; but that at certain points the development of fibrous tissue has taken place to such an extent that there are numbers of strongly marked fibrous bands intersecting the lobules and cutting up the liver tissue. These fibrous bands are highly vascular, and vessels at all stages of development are seen in their substance. In the fibrous band and around the vessels the first trace of the developing gumma is the appearance of a number of deeply stained embryonic cells, forming a ring which gradually increases in diameter, and as this extends peripherally, the cells near the centre become angular, granular, atrophied, and (stained with picro-carmine) yellow in colour.

In this stage the gumma is an actively growing mass of connective tissue, for it may be observed that around the embryonic cells at the periphery there is a delicate fibrillated stroma. Whilst the growth is going on in the gumma, certain changes are also to be observed in the vessels in the immediate neighbourhood. If one can be examined in transverse section, it will be at once seen that the walls are thickened, and that this increase in thickness takes place principally in the "intima," or within the internal elastic lamina (which in the picro-carmine stained specimen is bright yellow). In some cases this thickening of the "intima" is so great that the lumen of the vessel is almost entirely obliterated; and it is to be observed that even where the obliteration is not complete there is frequently a coagulum fixed in the lumen, which would prevent the passage of blood through the vessel.

High power (× 300).—The granular shrivelled cells in the centre of the mass are readily made out. They are small in size, and are closely packed together, and frequently are stained yellow, even before distinct caseation has set in. The larger embryonic cells towards

the periphery can now be readily discerned, and between them the fibrillated connective tissue basis, the nuclei of the peripheral cells, taking on the pink or logwood staining very readily. In the vessel, with the outer wall of which the gummatous growth is practically continuous, the endothelial cells of the "intima" have undergone enormous proliferation, and the flattened cells are arranged layer upon layer, until the lumen of the vessel is almost filled with them. The nuclei of these endothelial cells stain very deeply. Within the narrowed tube a coagulum of fibrin is frequently found, with a few white blood corpuscles at the periphery of the clot adhering to the wall. It appears to be highly probable that the caseation which almost invariably ensues in gummata in the liver is brought about (1.) by the contraction of the tissue at the periphery of the gumma itself and in the fibrous tissue surrounding it; (2.) by the *endarteritis obliterans* causing the stoppage of the vessel either alone or (3.) by the aid of a coagulum which forms on its roughened and inflamed walls. The change in the artery may take place at some point outside the gumma; but so long as the blood supply to the gumma is cut off the effect is the same—fatty degeneration of the tissues, followed by caseation, and later usually by absorption and cicatrisation. The section of the gumma is then hard and firm, and cuts almost like gritty indiarubber.

Where caseation has ensued, as in the gummata found in the adult, a section should be stained with picro-carmine (§ 73, p. 53), and one with osmic acid (§ 80, p. 62). Mount both in Farrant's solution.

Low power (× 50).—The centre of the mass is seen to be stained yellow, as the caseated material gives the yellow reaction with picric acid. Around the caseous portion is a distinctly fibrous zone, by the contraction of which is caused the indentation of the capsule of the liver at the outer margin of the growth. This fibrous capsule gradually shades off into the surrounding cirrhotic tissue, between the bands of which may be seen the Y-shaped trabeculæ of atrophied liver cells. The vessels in the neighbourhood have their "adventitia" thickened considerably, whilst the proliferation of the endothelium lining the vessel is also well marked.

High power (× 300).—The caseous yellow mass is seen to be made up of shrivelled granular *débris*, with bands of fibrous tissue running

in, apparently continued from the capsule. Crystals of cholesterin and of stearic acid are also frequently met with, and fat granules, or even

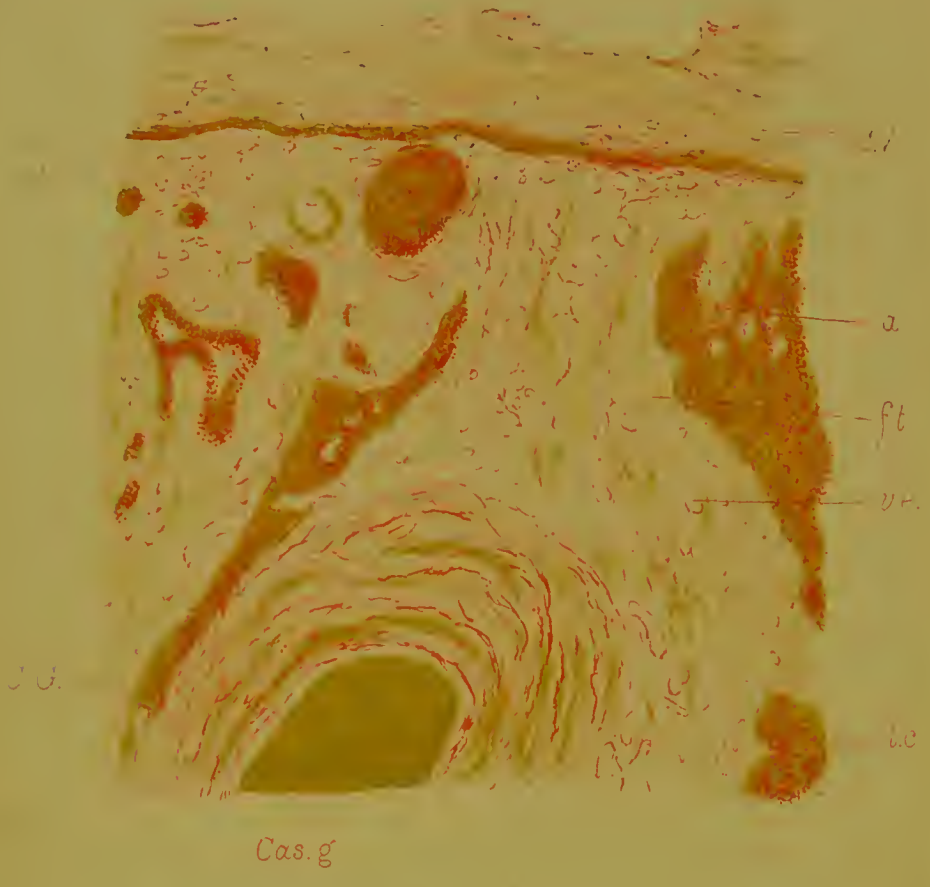


FIG. 28.—Drawing from a section of liver with hepatitis gummosa, stained with picro-carmine. (× 20.)

C.V. Thickened capsule, pink and fibrous in appearance.

A.A. Arteries becoming obliterated by thickening of both internal and external coats.

f.t. Continuation of the fibrous tissue from the capsule into the substance of the liver, in which are numerous sections of embryonic vessels (*v.e.*) seen.

l.c. Small patches of liver tissue left between the bands of fibrous tissue.

C.G. Fibrous external zone ; and *Cas. g.*, caseating central zone of softening gumma just below the capsule.

globules—readily recognised with the aid of osmic acid staining. In the fibrous capsule are seen under this power a number of lymph spaces which contain blackened globules, these being in all probability brought from the caseous mass. In this way the gumma may be gradually absorbed, as the fibrous tissue around is exceedingly vascular. Under this power the changes already described as occur-

ring in the neighbouring vessels may be again noted, as may also those described as being identical with the changes in syphilitic cirrhosis.

Another section should be stained with methylaniline violet (§ 76, p. 59), and mounted in Farrant's solution (§ 98, p. 71), in order that the condition of the middle coat of the vessels may be observed, for it is frequently found that this middle coat is undergoing the lardaceous or waxy degenerative change, so common a result of syphilis in its various forms.

It is difficult to look upon the whole process as anything more than a caseation of parts or areas of fibrous tissue, from cutting off of the blood supply, due to the *endarteritis obliterans*, as pointed out by Greenfield.

Syphilitic Cicatrices.

121. Syphilitic cicatrices appear to be the result of the two previous lesions. The liver may be cut up into a series of small masses by bands of fibrous tissue. These bands run in from a thickened capsule, the thickening being due to perihepatitis or inflammation of the capsule, as a result of which also the liver is found to be firmly adherent to the diaphragm. If a section is made through one of these fibrous bands, as a rule a number of small gummata are found scattered throughout the tissue. Harden in Müller's fluid (§ 53, p. 42), or spirit (§ 52, p. 42), stain with picro-carmine (§ 73, p. 53), and mount in Farrant's solution (§ 98, p. 71).

On examining under a low power (× 20) the cirrhosis is seen to commence at the surface of the capsule, and bands of pink fibrous tissue may be seen running irregularly through the organ. Between the bands of fibrous tissue, especially at the margins of the fibrous mass, are the thinned looking rows of atrophied liver cells as seen around gummata, and in the syphilitic cirrhotic liver. All this should be verified under the high power (× 300).

Acute Yellow Atrophy.

122. In the stage at which, in acute yellow atrophy, the organ comes under examination, the liver is found to be considerably atrophied; as a consequence of this the capsule is markedly wrinkled,

and may be caught up between the fingers. The organ is soft and flabby, in some cases almost fluid-feeling; the surface is of a uniform yellow ochre colour, or this may be replaced by a brownish tint. In a section the colour and appearances are much the same, and no traces of the individual lobules can, as a rule, be made out. Under the capsule are small punctiform hæmorrhages similar to those found on other serous surfaces in this condition.

On examining scrapings from the cut section (× 300) a number of liver cells in various stages of degeneration and atrophy are observed. They are almost invariably bile-stained, and granular in appearance; the nucleus is with difficulty distinguished, and in the protoplasmic substance are found numerous small granules of pigment. Along with these cells are a number of red and white blood corpuscles, crystals of leucin, tyrosin, and xanthin. (These may be seen in the blood and urine of the patient during life, and their presence appears to be due to the fact that the perfect oxidation of the proteid substances does not take place. So that these substances are formed as incomplete oxidation products.)

Harden a piece of the liver in absolute alcohol (§ 51, p. 42), cut (§ 67, p. 48), stain in carmine (§ 75, p. 58), and mount in Farrant's solution (§ 98, p. 71).

Low power (× 50).—Under this power it is possible to distinguish first of all a number of round cells (seen as pink nuclei) in the portal spaces, especially around the portal vein. There are evidences of an interstitial inflammation taking the form of an interlobular exudation. From the interlobular spaces and fissures, however, the process extends into the lobule between the columns of liver cells. Even under the low power small pink nuclei are to be seen in this position.

High power (× 300).—In the newly formed tissue a number of small bile ducts may be recognised as double rows of nuclei regularly arranged; some of them are pre-existing bile ducts enlarged, whilst others appear to be of entirely new formation. Under this power the liver cells may be seen to be atrophied, and of a yellow colour, even though they have no brown pigment. A great number of them, however, contain a considerable quantity of granular pigment, as noted above. The outline of the cell is angular, this angularity being due to the atrophy of the protoplasm. In a fresh section, in addition

to the above appearances, the crystals of leucin and tyrosin are readily distinguished. The pink nuclei (leucocytes and young connective tissue corpuscles) in the positions above mentioned can be recognised.

Tubercle of the Liver.

123. The liver is one of the best organs in the body in which to study the structure and development of tubercle, as in it the growth is uncomplicated by catarrhal changes, such as occur in the lung, whilst the formation of any fibrous tissue can be more easily traced and assigned to its proper cause.

The tubercular nodules are first seen as small grey or caseous granulations, either in the capsule itself, or near the surface of the liver. It is only in the very earliest stages that these tubercle masses are grey, for as soon as the growth has become fully developed, it is extravascular, and rapidly becomes first caseous, and then bile-stained.

A section of the liver with one of these small grey granulations is to be hardened in alcohol in the ordinary way (§ 42, p. 51); and sections are to be stained in picro-carmine (§ 73, p. 53), and mounted in Farrant's solution (§ 98, p. 71).

Examine under a low power (× 50). In one of the interlobular spaces, or just at the margin of a lobule, is seen a granular looking mass pushing aside the liver cells, and apparently infiltrating gradually. This mass has a more or less pink colour. Towards the centre is a bright orange ring, about the size of a small pin's head, which surrounds a light canary yellow centre.

Under a high power (× 300) the elements of which the tubercle follicle is composed may be made out. At the periphery of the growth, and spreading in between the liver cells, are numerous small round cells, taking on the pink staining, and appearing to be little more than young connective tissue nuclei; nearer the centre, or rather running amongst the inner layers of these small cells, is a somewhat dense, felted mass of fibrous tissue, staining pink, though in some cases, especially where the growth is still young, there appears to be very little of the fibrous tissue. As the centre is neared, the tissue opens out into a kind of network, in the meshes of which are found a number of larger cells of

various shapes. Many of them contain two, three, or even more nuclei. These appear to be endothelioid cells, such as are found lying on all bundles of connective tissue, especially such as grow rapidly. The centre of the tubercle is occupied by the so-called giant cell, which is

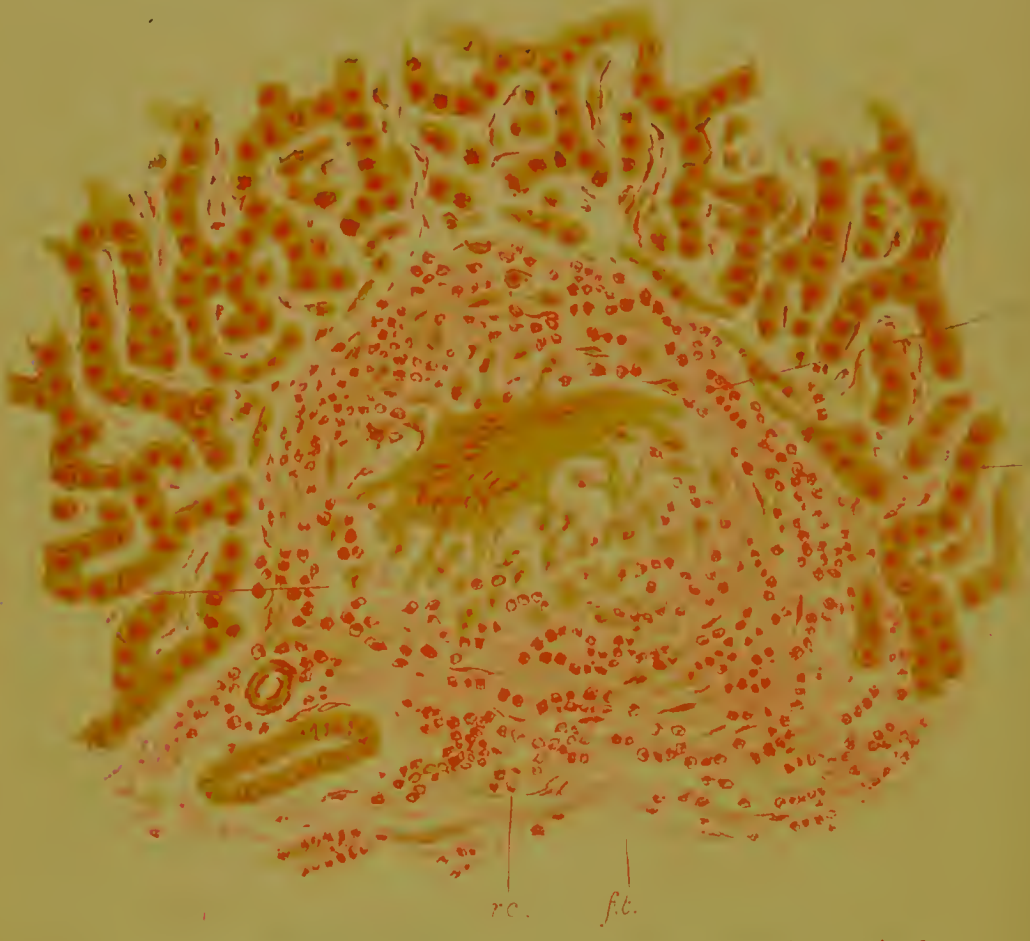


FIG. 29.—Drawing from section of tubercle of the liver, stained with picro-carmine. (× 300.)

g. Giant cell, with nuclei at the periphery, and sending off branching processes.

e.c. Endothelioid cells, lying on fibrillæ of the network of connective tissue, with which the branching processes of the giant cell appear to anastomose.

r.c. Round cells, young connective tissue corpuscles appearing towards the periphery of the mass.

f.t. Fibrous tissue, forming a kind of capsule to the tubercle. In this capsule are a number of the rounded nuclei.

l.c. Columns of liver cells, those near the tubercle somewhat flattened and atrophied; between them are rounded nuclei, &c., extending from the growing tubercle mass.

b.d. Small bile duct. *a.* Branch of hepatic artery.

seen as a large branching cell, from the periphery of which processes run to join the fibrous reticulum (Fig. 29). In the liver these processes

can often be very distinctly seen. At the periphery of the cell are a number of rounded, deeply stained bodies, which are about the size of the small cells found at the periphery of the tubercle, but they appear to be somewhat more deeply stained. They form a distinct belt or zone around the cell, as a single or double row, and they bound the bright canary yellow material already spoken of; this occupies the body of the cell, and is, as a rule, perfectly homogeneous and translucent.

The tubercle follicles (each giant cell system), as they are called, are developed, as noted above, in the interlobular or portal spaces. Around the primary follicle may be formed numerous other follicles which, being also extravascular, cut off the supply of nutriment from the central part, which rapidly undergoes death and caseation. At the same time the small bile ducts are involved, and bile is poured into the caseous material, from which fact it is found that tubercle in the liver, except in the very earliest stages, is invariably of a greenish yellow colour (all dead matter in the liver becoming bile-stained).

These tuberculous masses may gradually enlarge, forming yellowish green masses of considerable size, the centre always caseating and softening, until at length large cysts may be formed, the walls of which are fibrous or gelatinous looking—(in this gelatinous looking wall are found numerous tubercle follicles)—whilst contained within this fibrous capsule is a green soft putty-like mass, which, on microscopic examination, is found to be made up of granular *débris*, fatty globules, and angular shrivelled and atrophied cells. In certain cases the caseous material is replaced by a clear watery fluid, which appears to be bile from which the bile acids, pigments, and salts have been absorbed. Around all the bile ducts lymphatics are found in great numbers, and this fact may account for the special affection of the bile ducts by the tuberculous growths.

In one form of tubercle the larger bile ducts are specially affected. If the wall of the bile duct be examined in such a case, a growth of tubercle follicles is found in the submucous layer; this rapidly undergoes caseation, and ulceration ensues, as the blood supply from the epithelium is cut off by the non-vascular tubercular growth beneath. The process extends along the lymphatics, and so the tubercle spreads; but it also spreads by direct infection, by application of the specific material to opposite or even distant

surfaces. This form of tubercle should be studied along with tubercular ulcer of the intestine and tubercular pyelo-nephritis, both of which it in many respects closely resembles. Very frequently other conditions are found associated with tubercle of the liver, such as cirrhosis—which is especially met with in the livers of tuberculous children—waxy changes in the vessels, fatty infiltration or degeneration of the liver cells, accompanied in the latter case by atrophic changes and shrivelling of the cells; so that in examining a tubercular liver these complications should be borne in mind, and such changes carefully searched for and noted.

A peculiar lymphoid growth, very similar to the above in many respects, apparently differing only in the fact that it contains no giant

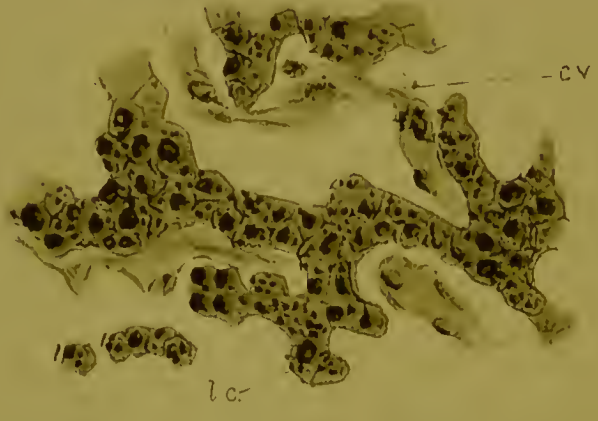


FIG. 30.—Drawing of liver cells undergoing fatty degeneration, taken from near the centre of a lobule. Stained with osmic acid. (× 300.)

l.c. Liver cells arranged in columns. The outlines of these cells are very distinctly marked, the nucleus is not visible in most of the cells, which are small, and have in their protoplasm several droplets of fat, these droplets varying very much in size, but are usually comparatively small.

c.v. Capillary vessels and delicate connective tissue, the nuclei of both of which are seen slightly stained by the osmic acid.

cells, is also sometimes met with in the liver. Prepare in alcohol (§ 51, p. 42), cut (§ 67, p. 48), stain a section in picro-carmine, and examine under the low power (× 50). The granular looking pink-stained mass is seen lying in the interlobular spaces, but no orange ring can be made out in the centre. The liver capillaries appear to be relatively much enlarged, whilst the rows of liver cells are thinned and appear irregular (Fig. 30). In an unstained specimen, small, bright, strongly refractile bodies are observed, even under the low

power, and those in a specimen stained with osmic acid (§ 80, p. 62) are blackened.

Under the high power (× 300) the granular pink mass is seen to be composed of rounded cells, small at the periphery, whilst nearer the centre they are larger, multinucleated, and in some instances irregular in shape. Running throughout the mass are strands of delicate pink-stained fibrous or reticular tissue, and larger cells appear to be lying on these strands. The liver cells are distinctly atrophied and angular, the nucleus is with difficulty discerned, and the protoplasm of the cell appears to be partially converted into fatty globules, which are seen as highly refractile or blackened bodies (Fig. 30), according as they are examined unstained or stained with picro-carmine or osmic acid. In some of the cells there is an appearance of vacuolation, which is probably due to the presence of fatty globules, as already described. This condition is met with where there are like changes in any of the lymphatic glands of the body, changes in which the naked eye appearances are similar to those met with in tubercle.

Lymphadenoma of the Liver.

(*Hodgkin's Disease.*)

124. In Hodgkin's disease the organ is enlarged, smooth, and pale (Greenhow, in "New Sydenham Society Atlas"), and the growths usually occur as small, pale pink or grey nodules, which are seen specially affecting the portal canal, spreading thence into the substances of the lobules. They may be numerous or few in number. Sometimes the masses are larger, when they assume a "greyish yellow colour," and are tough, but in some cases they are undergoing caseation and softening. Each of these masses, varying in size from a pin's head to a sixpence, is surrounded by a zone of reddened tissue, which appears to be made up of dilated venous capillaries. There is a different form, or a more advanced stage, where grey streaks appear both on the surface under the capsule and on the surface of a section. This condition of the liver is almost invariably associated with a similar condition of other organs—spleen, kidney, &c. &c., with induration and enlargement of the lymphatic glands. Harden in

Müller's fluid (§ 53, p. 42), cut sections (§ 67, p. 48), and stain one with picro-carmine (§ 73, p. 53). Observe that the appearances described under the head of lymphoid growth are here repeated, commencing in the portal spaces, and gradually extending into the substance of the lobule running from the periphery towards the centre, apparently along the walls of the capillaries, the endothelial cells of which become increased in size, and are often multinucleated. The growth consists then of a network of fibrous tissue stuffed with leucocytes, connective tissue, or lymphoid cells and endothelioid plates, and at the margin of the growths the liver cells have undergone atrophy.

Leucocythemia of the Liver.

125. In this condition the liver is usually enlarged, in some cases considerably so; the surface is smooth and pale. On section, a pale

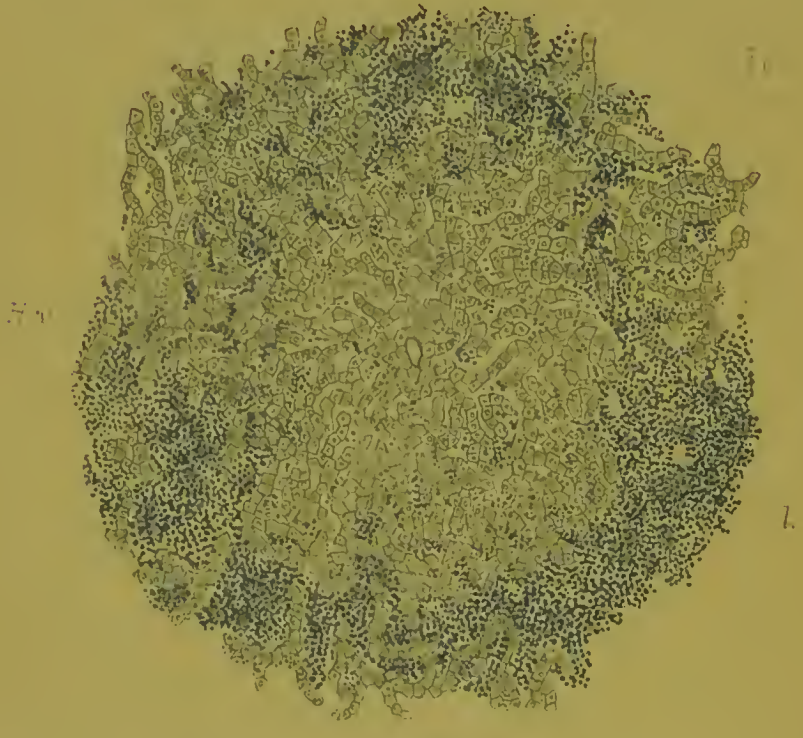


Fig. 31.—Section of leucocythemic liver stained with logwood. (× 70.)
H.v. Central or Hepatic vein.
l. Leucocytes, especially numerous at the periphery of the lobule.
l.c. Rows of liver cells between capillary vessels.

smooth surface is seen, whilst between the lobules, or in the interlobular fissures and spaces, the pallor is more distinctly marked, so that

on the surface of a fresh section there is an "irregular veining of pearly-white colour," and the tissue enclosed in this network is more or less anæmic looking. The whole organ is firm and fleshy-feeling to the touch.

Harden a piece of the organ in Müller's fluid (§ 53, p. 43), or in spirit (§ 52, p. 42); stain a section with logwood (§ 74, p. 57), and mount in Canada balsam (§ 96, p. 69).

On examining under a low power (× 50), it is to be observed that in the interlobular spaces and fissures there are enormous numbers of deeply stained nuclei, by which the lobules are very distinctly marked out. Masses of these nuclei also run for some little distance into the lobule (Fig. 31), and the intercolumnar capillaries are crowded with nuclei or leucocytes. In addition to this crowding of the vessels there is an exudation of leucocytes into the spaces and tissues surrounding the vessels.

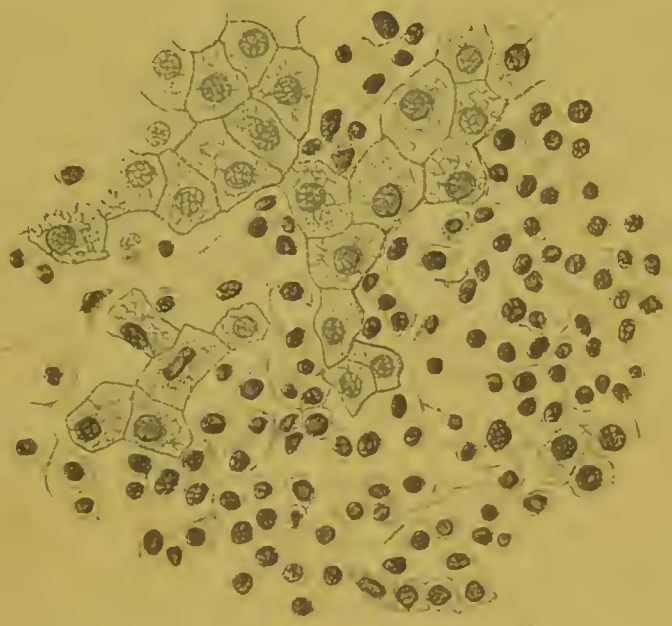


FIG. 32.—Section of leucocythemic liver, taken from the periphery of a lobule, stained with logwood. (× 600.)

l.c. Liver cells, with intranuclear and intracellular plexus.

f. Strands of fibrin between (*l.*) leucocytes and (*c.t.*) connective tissue corpuseles.

e.c. Large round cells with two nuclei.

Under a high power (× 300) the infiltration around the vessels is more distinctly made out, and the capillaries are seen to be crowded

both inside and out with the deeply stained cells, so that in many places the liver cells appear to be atrophied, and even destroyed, by the pressure of these deeply stained cells or leucocytes, though otherwise they remain unchanged.

The small cells, when carefully examined with this power, are in all respects like the so-called wandering cells or leucocytes, and are surrounded by no stroma of any description, except a few delicate threads of coagulated fibrin lying in the normal connective tissue of the part, in this respect differing very markedly from the condition described in lymphadenoma, where a distinct stroma or network was observed, in which were found the small round cells, and also the larger endothelioid cells.

Typhoid Lesion.

126. There is a condition of the liver induced in typhoid fever of long-continued standing and of severe type, which it is necessary to mention, though it is probably a condition common to this and other diseases, and appears to be a peculiar inflammatory change due to some septic infection, or embolism occurring in the venules of the intermediate zone of the lobules. In addition to the general cloudy swelling of the liver cells, scattered throughout the substance of the liver, are found a number of small yellow specks about the size of a pin's head, situated in the position mentioned, or in some cases involving the whole of the lobule. Where this change is observed, the organ should be hardened in absolute alcohol (§ 51, p. 42); stain a section with picro-carmine (§ 73, p. 53), and mount in Farrant's solution (§ 98, p. 71).

Low power (× 50).—Note that parts of some of the lobules are more deeply stained than the surrounding liver tissue. These deeply stained patches are not met with in every lobule, but only here and there, one or two comparatively normal lobules intervening between the affected areas.

High power (× 300).—One of two conditions will be observed in the affected portions. In the early stage there is extreme cloudy swelling of the liver cells. They are markedly swollen and compressed, so that the outlines are not distinctly discerned. The protoplasm of the cells is extremely granular, and by the extreme granularity and the opacity

of the protoplasm the nucleus is frequently somewhat obscured, or even lost sight of. The cloudy swelling is more or less marked in the cells of the whole of the lobule, but is most characteristic in the situations mentioned. In the later stages the protoplasm of the liver cells appears to undergo complete disorganisation; and in this change the nucleus takes part, so that in the intermediate zone of each lobule only a mass of granular *débris* is to be seen. The mass takes on the pink staining somewhat distinctly, unless it has been in this condition for some little time before the death of the patient, in which case it takes on more of a yellow stain (with picro-carmine), as do all necrosed tissues. This condition appears to be similar to that which is met with in the liver in some cases of dysentery, where there is commencement of formation of abscesses in the liver.

Another lesion described by the German pathologists as occurring in similar conditions—in typhoid fever, scarlet fever, measles, and other specific fevers—is a tubercle-like growth, or, more precisely, a cellular infiltration, occurring in the portal canals and in the course of the inter-columnar capillaries. These are also probably the early stages of small abscess formations, and are due to cell proliferation and infiltration. They differ but slightly in position from those described under the heading "typhoid lesion," and in other respects their characteristics are very similar.

Abscesses of the Liver.

127. (1.) *Tropical Abscess.*—A form met with in hot climates, occurring as a single abscess (or at most two or three), deeply situated in the right lobe of the liver. The walls of the cavity are ragged, and shreds of liver tissue are found hanging into the cavity. There is no trace of a membrane, or even of a condensation of the surrounding tissues. On examination of the contents of the cavity they are found to consist of a creamy, pus-like material, tinged pink by the presence of a small quantity of blood: this matter has a peculiar characteristic odour, but is not putrid. On examination of the fluid in a neutral solution (¾ % salt, § 34, p. 32) numerous pus corpuscles are found, which are cleared up by the addition of a drop of acetic acid, and several nuclei are made evident; mixed with the corpuscles are seen *débris*, consisting of liver cells in various stages of disintegration, delicate

shreds of connective tissue, and very frequently numerous red blood corpuscles. Around the abscess there is no sign of inflammation. It appears as though the liver tissue was simply broken down completely around one focus, without any hyperæmic or surrounding inflammatory changes.

(2.) *Pyæmic Abscess.*—Is comparatively rare in the liver, unless there is some source of putrefactive infection in the tract from which the portal blood comes—such as a putrid ulcer of the mucous surface of the stomach or intestinal canal, or septic disease of the abdominal organs, uterus, rectum, &c.; or, again, it may be caused by phlebitis, due to the presence of a calculus in the portal vein. In all these conditions there is absorption of some septic material from the primary infecting source by the portal vein. It is said, too, that in injuries to the cranial bones, where there is suppuration extending to the open veins of the diplöe, there is a tendency to the formation of pyæmic abscess; but this has been denied by several authors, who have examined numerous cases of this form of disease or of injury of the cranial bones.

Such abscesses are usually small and multiple, and are more or less wedge-shaped. They appear to be limited to certain branches of the portal vein, and are found especially near the surface of the organ. On opening into them, a quantity of very foul smelling, ash grey or greenish pus is evacuated, which, treated with acetic acid and examined, is found to be made up of ordinary pus corpuscles and shreds of tissue in the last stages of disintegration. Harden a piece of the liver near the abscess and a part of the wall in absolute alcohol (§ 51, p. 42), and stain a section in picro-carmine (§ 73, p. 53). The walls of the abscesses are sloughy and ragged looking, and are infiltrated with great quantities of pus corpuscles or round cells, whilst surrounding this sloughy and sodden zone is an area or zone which appears to be highly injected and vascular. Around the vessels in this position there are numerous leucocytes stained pink with the picro-carmine. These abscesses are probably the result of septic inflammatory changes in the corresponding branches of the portal vein, in which are found septic thrombi. Stain a section with methylaniline violet (§ 76, p. 59), mount in Canada balsam (§ 96, p. 69), and look for micrococci, which are frequently met with

in this condition as violet stained granular looking masses, in some cases forming a considerable part of the "clot" in the vessel. There is, in fact, a condition similar to that described under the heading of typhoid lesion. In both of the above abscesses, whether in the single or the multiple form, it is to be noted that the walls are sloughy and that there are ragged shreds of tissue projecting into the abscess cavity. This is an important diagnostic point, for in the next form of abscess it will be found that the walls are usually smooth and well defined.

(3.) *Suppuration in Hydatid Cyst of the Liver.*—Where suppuration takes place in a hydatid cyst as a result of direct violence, or from any other cause, the hydatid membrane becomes swollen, and may be entirely broken down and evacuated, but even then the false fibrous capsule formed by the condensed tissue of the organ remains for a considerable time, and bounds the cavity as a smooth, well-marked wall; in addition to which hooklets are generally to be found in the discharge, distinguishing it from either of the above forms.

Cysts of the Liver.

128. (1.) Hydatid cysts, generally found as a single cyst, or at most two or three, in the right lobe of the liver.—(See Hydatid Cysts under "Parasites.")

(2.) Simple serous cysts. As a rule, single; probably due to the distentions of a bile duct, often by obstruction by pressure of a cancer or some similar growth. As from all collections of bile in the liver, the bile salts, acids, and colouring matter are gradually absorbed, and a clear fluid is left.

(3.) Similar cysts formed by the distention of bile ducts resulting from tubercular growth in their walls. These have a soft, caseous, and somewhat ragged lining.

(4.) True cystic disease of the liver, associated with a similar condition of the kidney. The cysts vary in size from microscopic spaces to cavities the size of a walnut. The walls are thin, smooth, and fibrous, and within the cavity a clear watery or serous fluid is collected. The mode of origin of these cysts is somewhat doubtful, some holding that they are formed by vacuolation of the liver cells, whilst others maintain that they are dilated bile ducts, the dilatation

being caused by constriction of the ducts at certain points by a growth of fibrous and non-striped muscular tissue.

(5.) A form of cyst said to be due to *post mortem* decomposition, occurring especially in hot weather. In this form the liver tissue is converted into a kind of cavernous tissue by the rapid formation in its substance of putrefactive gases.—(Moxon, Goodhart.)

Angioma of the Liver.

129. This tumour is not yet very frequently met with in the human subject, but in the liver of the cat it is of common occurrence. When present it is, as a rule, found near the surface, and may be seen shining through the capsule as a purple or dark claret coloured patch. The patch may be single, and about a third of an inch in size; but frequently the growth is multiple. At the site of the tumour is a slight depression, and the tumour has the appearance of an extravasation of blood sharply defined from the surrounding

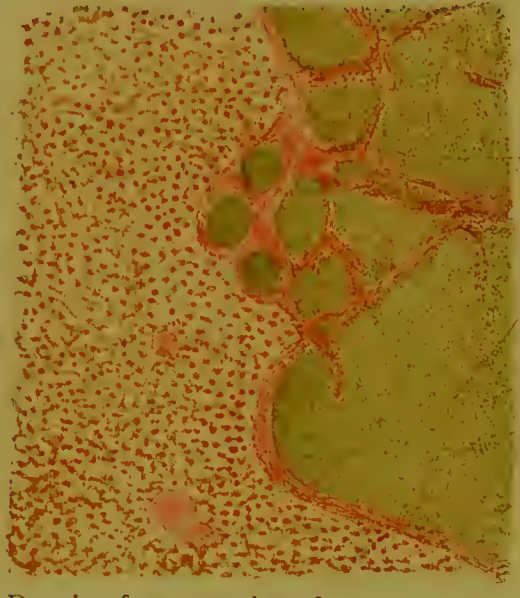


Fig. 33.—Drawing from a section of a cavernous angioma of the liver, stained with picro-carmine. (× 50.)

c.a. Fibrous capsule marking the angioma off pretty sharply from the normal liver substance, *l.*

f.t. Fibrous trabeculæ running from the capsule into the substance of the tumour, forming spaces (*c.s.*) lined with flattened nucleated cells, and containing apparently nothing but blood, coloured and colourless corpuscles.

tissues, though it can be injected from any of the vessels of the liver. On making a section, after hardening a piece of the liver in which the

tumour occurs in Müller's fluid (§ 53, p. 42), the tumour is seen to be round or wedge-shaped, and is sharply marked off from the liver tissue, and at first sight appears little more than a mass of coagulated blood. Stain a section in picro-carmine (§ 73, p. 53), and mount in Farrant's solution (§ 98, p. 71).

Low power (× 50).—Around the tumour, and circumscribing it sharply, as already seen, is a more or less fibrous capsule, in which are numerous pink-stained nuclei. Running in from the capsule are seen bands or trabeculæ of similar fibrous tissue, stained pink, with the nuclei of a deeper tinge. The bands form a kind of network, the spaces or meshes of which communicate with one another. In these spaces under this power a granular looking greenish mass (Fig. 33) is seen, with here and there a small pink dot. This is the blood which fills the cavernous structure.

Under a high power (× 300) the fibrous capsule and trabeculæ,

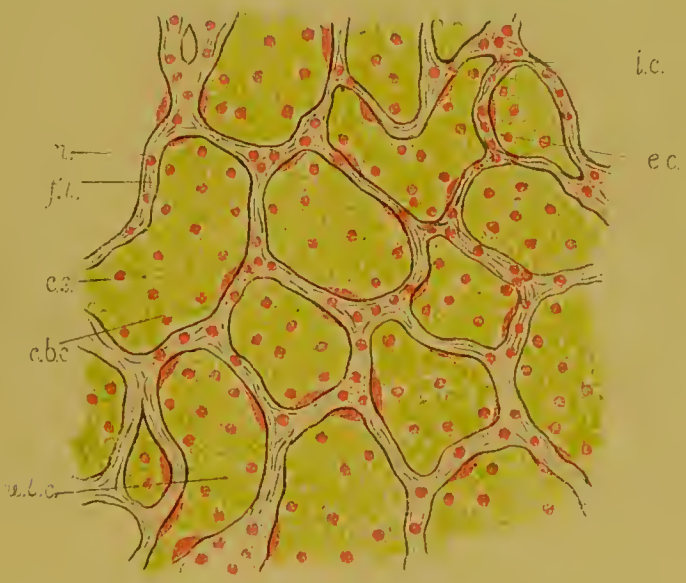


FIG. 34.—Drawing from a section of cavernous angioma of the liver, stained with picro-carmine. (× 300.)

f.t. Fibrous trabeculæ surrounding (*c.s.*) cavernous sinuses.
l.c. Nuclei of liver cells between sinuses, (*n.*) connective tissue nuclei.
e.c. Endothelial cells lining the sinuses, and in contact with
c.b.c. The coloured and (*w.b.c.*) the colourless blood corpuscles.

stained a delicate pink, may be distinguished, with a considerable number of more deeply stained nuclei, or young connective tissue

corpuscles, lying amongst or in the fibres. In some of the trabeculæ a few atrophied liver cells may be met with, apparently enclosed and compressed between the bands of fibrous looking tissue ; but in most of the bands no such cells are to be met with. Lying on the bands of fibrous tissue, and apparently lining the cavernous spaces, are a number of endothelial flattened cells, which, seen in section, are spindle-shaped, and in which are one or more rounded nuclei. These cells have very much the appearance of the endothelial cells forming the smooth lining surface of blood-vessels. Lying in the cavities are numerous coloured blood corpuscles stained of a quaker green colour, whilst here and there may be seen a pink-stained cell, which will at once be recognised as a colourless blood corpuscle. These tumours appear to be formed by the dilatation of capillary vessels and atrophy of the intervening liver cells. The walls of the vessels become thickened, but in some places they give way, and additional intercommunications are thus formed. It appears, in fact, to be a very advanced but similar condition to that met with in "nutmeg liver" (§ 116, p. 94).

Other Tumours of the Liver.

130. Tumours of the liver are similar in their structure to those found in other parts or organs of the body, so that here it will be necessary only to state what tumours may occur in this organ, and to give one or two naked eye characteristics of the different forms of tumour growth.

Cancers may be either diffused or nodular. In the diffused form the liver is usually much enlarged. Throughout the organ there is a peculiar veining or mottling, caused by the presence of bands of glue-like material, very like the bands of young fibrous tissue seen in certain forms of cirrhosis, more especially to the naked eye, and in some cases even under the microscope. On more careful examination, however, these bands are found to have a more or less characteristic carcinomatous structure. Of the nodular forms the harder masses, sharply defined from the surrounding tissues, rounded but umbilicated in the centre, pink at the periphery, and yellower towards the centre, with, in some cases, fatty looking patches, and but few hæmorrhagic points,

are generally cancerous. In some cases somewhat firm nodular sarcomatous masses are met with. These, however, are rare, and may generally be recognised by the greater number of small hæmorrhages.

The softer nodules occurring in the liver may be either cancerous or sarcomatous, and they both occur in an enlarged liver. They are of rapid growth, and are somewhat sharply circumscribed; they project from the free or from a cut surface, are pink in colour, and frequently are somewhat translucent looking. The only point of difference here is that, in the sarcoma, hæmorrhages are much more frequent, taking place into the tissues of the tumour; in consequence of which, red, brown, or yellow patches, according to the date of the hæmorrhage, are scattered throughout the substance of the tumour.

Malignant pigmented tumours of the liver are invariably sarcomatous. Beyond the evidence to be derived from these general facts, it is, as a rule, impossible to collect with the naked eye any which will enable one to state with any degree of certainty what the nature of the tumour is, until a careful histological examination has been made.

For the method of conducting this examination see section on Tumours.

CHAPTER IV.

THE HEART.

Microscopic Structure of the Wall of the Normal Heart.

131. If a section be made through the wall of the left ventricle, and a thin layer of the tissue, embracing both the outer and inner surfaces, be prepared for microscopic examination, the following appearances may be made out with the low power (× 50). The epicardium, or visceral layer of the pericardium, is seen as a mass of pink tissue (if the section has been treated with carmine or picro-carmine), much more dense at its outer surface than near the muscular tissue, where it appears to be more in the form of an open connective tissue network, with small pink nuclei scattered throughout its substance. Bounding the muscular tissue is a layer of connective tissue, the cells of which have become infiltrated with fat. This layer of adipose tissue varies considerably, but is almost invariably present, though sometimes it is exceedingly thin. In the more open part of the pericardium, the open mouths of vessels are readily seen, and by special preparation the presence of numerous nerves and lymphatics may be demonstrated. Beneath the pericardium are numerous bundles of yellowish-brown muscular tissue (when the section is stained with picro-carmine); in these bundles pink-stained nuclei appear scattered irregularly throughout the tissue. Bands of pink connective tissue run between the larger bundles of muscular fibre, forming a kind of supporting framework for the muscular tissue. The muscular bundles are seen both in longitudinal and transverse section. Where seen in the former they appear to form a peculiar reticulated mass of fibres, the openings between the reticular strands in some cases appearing to be of considerable size.

Passing to the endocardial surface, small elevations or irregularities are observed, which are the sections through some of the musculi papillares. The endocardium itself under this power appears to consist of a very thin layer of connective tissue, with here and there throughout its substance a few *small* bundles of muscular tissue.

Under the high power (× 400), the epicardium is seen to consist of ordinary connective tissue, condensed near the surface, with bands of yellow elastic tissue in the condensed part. Covering this is a single layer of flattened nucleated endothelial cells, which, seen in section, appear to be spindle-shaped ; and beneath, as already seen under the low power, is a quantity of opener and more vascular connective tissue, in the deeper part of which are found the fat cells with their "signet-ring" appearance, the nucleus in the angle of the cell being supposed to represent the seal.

The muscular elements of the heart resemble those of ordinary striped or voluntary muscle, in that they are distinguished by having both longitudinal and transverse striation. Each fibre is composed of a series of muscle elements, which, in turn, are made up of three factors :—(1) a nucleus containing an intranuclear plexus ; (2) a thin film of what usually appears to be more or less granular protoplasm, the two together forming the muscle corpuscle of Max Schultze, which is placed in the centre of (3) the mass of striated contractile formed material, or the functionally active part of the substance of the heart. This formed material, on the addition of a forty per cent. solution of caustic potash (§ 66, p. 47), or twenty per cent. solution of nitric acid (§ 66, p. 47), is broken up into a series of areas, each area being more or less cylindrical in form, and having for its central point a muscle corpuscle. It has, too, its extremities serrated, and in many cases at least one of its ends is bifurcated, each branch joining the serrated end of another, or part of another, cylinder. When a number of these branching cylinders are examined *in situ*, it is at once seen that they form the peculiar reticulated mass of fibres above referred to, and on making a transverse section the great difference in the sizes of the areas of the fibres is observed, as in some cases the whole section of a fibre is seen, whilst in others the section of one of the branches only is seen. Nuclei are to be made

out in the transverse as well as in the longitudinal section occupying the centres of the fibres, but are seen only when the section happens to pass through the muscle "cell." If it passes through one of the branches only, or through the end of the cell, the nucleus naturally cannot be seen through the mass of formed material. At the poles of these nuclei (especially when the heart is from a subject somewhat advanced in years) is seen a small quantity of golden yellow or brown pigment.

Around the muscular fibres of the heart there is no sarcolemma, so that the highly vascular connective tissue which lies in the interstices of the muscular network is in direct contact with the muscular elements.

The connective tissue, in addition to having a rich vascular supply, is completely excavated by lymph spaces and lymphatic vessels. The nuclei of these various tissues are readily seen in sections of the muscle of the heart, stained with logwood (§ 74, p. 57) or carmine, and mounted in Canada balsam (§ 96, p. 69).

Under this power the endocardium should be seen to have on its inner surface a single layer of flattened nucleated or endothelial cells. In the human heart this layer is seldom seen, as the organs are not as a rule removed within twenty-four hours after death, by which time the endothelial cells have disappeared. Beneath this layer is a network of flattened branched cells lying on a mass of elastic tissue, and from it trabeculæ are sent to join the connective tissue between the muscular fibres, whilst in its substance are to be found muscular bands which, though small, are in all other respects similar to those of the myocardium.

Cloudy Swelling.

132. Cloudy swelling of the muscular fibres of the heart appears to be an early stage of either an inflammatory condition of the myocardium or of the following condition of fatty degeneration. It may then be said to be the result of an inflammatory condition maintained for a short time, or, in some cases, it may be looked upon as the precursor of fatty metamorphosis of the muscular tissue. It frequently occurs during the course of certain specific or organic fevers, where the temperature is raised to a considerable degree, as in typhoid fever,

scarlatina, septicæmia, and the rest. In one case a severe burn, causing death in six hours, is recorded by Weber as having induced this condition in the muscular fibres of the heart and in the epithelium of the tubules of the kidney. It is in such cases that this condition must be looked for.

Naked eye appearances.—A heart so affected is not so firm and tough as is the normal heart. Its muscular wall is somewhat softened, and in some cases becomes even friable, and may be broken down by squeezing between the tips of the fingers and thumb. The tissue is of a dirty grey colour, in place of the usual purple red, and appears as though it had been slightly boiled—(Perls). A fresh section of the muscle presents the same grey colour, and has a peculiar translucent appearance. The endocardial surface seems to be the part which is specially affected by the disease, as will be seen when the microscopical examination is made. Take a piece of the muscular tissue from the left ventricle about three-quarters of an inch square, and harden in Müller's fluid (§ 53, p. 42). Make sections, and prepare one unstained in a drop of neutral solution (§ 34, p. 32); another stained in osmic acid (§ 80, p. 62), and mounted in Farrant's solution; a third in picro-carmine (§ 73, p. 53), and mounted in Farrant's solution; and a fourth in logwood (§ 74, p. 57), and mounted in Canada balsam (§ 96, p. 69).

Under the low power (× 50), examining the longitudinal section of the fibres, it will be seen that the spaces between the individual fibres of the network are somewhat smaller than in the normal heart. Even under this power the tissue looks slightly opaque. Search for a thin part of the section and centre it.

Examine under the high power (× 400). In the unstained specimen the fibres are seen to be somewhat opaque. The transverse striation, which in the normal fibre is so readily made out, is here somewhat obscured, and in place of it there appears a granularity of the whole of the formed material or striated material of the muscle element. The granules are exceedingly minute, and the appearance of the striated muscle is described as seen through a thin layer of dust or a sheet of ground glass. In such cases the nucleus is invariably more or less obscured, and sometimes cannot be made out at all.

If instead of the neutral solution a drop of water is added to a few of the fibres spread out on a slide, the granular cells break up, and



FIG. 35.—Muscular fibres of the heart in a state of cloudy swelling, stained with piero-carmine, and mounted in Farrant's solution. (× 300.)

c.s. Part of fibre in a condition of advanced cloudy swelling; transverse striation quite lost.

t.s. Indistinctly marked transverse striation.

f.c. Commencing formation of small fat globules.

the nucleus then becomes distinctly visible. Again, if a drop of acetic acid is run under the cover glass from the edge, the granular appearance fades away, and an almost normal looking fibre remains.[1]

Ether, chloroform, or strong alkalies run under the cover glass in the same manner leave the cloudiness unaffected.

Examining the osmic acid stained specimen, nothing is found which cannot be made out by the above methods, as with this reagent there is no blackening of the fine granules, from which fact it is to be inferred that they are not of a fatty nature.

With picro-carmine or logwood the muscular elements are not at all deeply stained, and these stains are principally useful for bringing into prominence the nuclei of the interstitial tissue and of the muscle corpuscles, which make their appearance in the course of a day or two in a few of the fibres. The nuclei of the connective tissue are frequently found to be more numerous and more distinctly stained than in the normal heart, especially where the condition arises during the course of an early inflammatory process. They are then seen as deeply stained bodies lying between the bands of muscular fibres,

[1] If a heart in which there is cloudy swelling (especially in the early stages of the condition) be kept in alcohol for some time, the cloudiness may become invisible, or nearly so. The alcohol appears to abstract water from the tissues, or otherwise so changes the protoplasm as to restore the refractive indices of the various elements to the normal.

arranged most frequently along each side of what appear to be the walls of small blood-vessels.

This cloudiness of the fibre is not equally distributed throughout the wall of the heart, but is much more advanced in some places than others. This is specially well marked where the cloudy swelling is to be looked upon as the precursor of fatty degeneration. (See next section.)

Fatty Infiltration of the Heart.

133. Fatty infiltration of the heart, or Adipose Heart, must be carefully distinguished from fatty degeneration of the muscular walls of the heart. In fatty infiltration there is at first simply an increase in the amount of the pericardial fat already referred to (§ 131, p. 130). Subsequently, the fat extends from the pericardial surface into the muscular substance of the organ between the various bands of fibres. Although the two processes of fatty infiltration and fatty degeneration are frequently associated (as in cases where the pressure of the invading adipose tissue on the muscular fibres brings about degeneration of these fibres), it will be well to describe the two separately.

The adipose heart, as seen with the naked eye, appears to be larger than normal, the increase in size being mainly due to an increase in the amount of subpericardial fat, though in the majority of cases there is also some flabbiness of the muscular tissue, more especially of the muscle near the outer surface. Small yellow streaks run down in the somewhat pale muscular tissue, evidently merely continuations of the adipose tissue from the subpericardial layer. Unless there is also fatty degeneration, the flabbiness does not extend beyond the gross lines of fatty tisue.

Harden a piece of the heart in Müller's fluid (§ 53, p. 42), make sections, and mount two sections in Farrant's solution (§ 98, p. 71), one stained in osmic acid (§ 80, p. 62), and the other in picro-carmine (§ 73, p. 53).

Examine under the low power (× 50). The pericardial tissue is found to be completely infiltrated with fat globules, which even under this power appear to be of considerable size. The connective tissue corpuscles have become filled and distended with fat, and now present the appearance of fat cells in adipose tissue; whilst the highly

refractile bodies have a double outline, and are stained black in the osmic acid specimen. The nucleus is situated at one angle of the cell, and is stained pink or olive green, as the case may be. These large cells are seen extending in rows down for some distance between the muscular fibres, but it is to be observed that they are entirely outside the fibres; that the condition is, in fact, one of fatty infiltration of the connective tissue framework of the heart, and not of the muscular substance proper. In very extreme cases this infiltration of the connective tissue cells with fat may advance as far as the endocardial surface, in which case, however, it is invariably associated with fatty degeneration.

High power (× 400).—The structure of the cells of the adipose tissue can now be made out more readily; they are closely packed together, but the following parts may be observed in each of them. The protoplasm of the cell forms a mere film, except at one point or angle, where there is generally a more or less triangular mass of protoplasm, in which is situated a nucleus stained as above, and seen very distinctly. Within the thin wall of protoplasm is a large globule of strongly refractile substance with a double outline, clear in the centre, and with a dark ring at the margin, or the reverse, according to the focus in which it is placed. With picro-carmine the globule remains unstained, but with osmic acid it is stained black. Between the muscular fibres they have exactly the same appearance, and in no way affect the fibre itself, except by actual mechanical pressure. As before stated, this condition must be carefully distinguished from fatty degeneration, which is an affection of the muscle substance proper.

Fatty Degeneration of the Muscular Wall of the Heart.

134. This condition is found in patients who have succumbed to various exhausting diseases, such as phthisis, anæmia, leucocythemia, Addison's disease, and disease generally in which there is an altered condition of the blood. It occurs also as a sequel to scarlatina and diseases of that type, or to such conditions as are in all probability due to septic poisoning; and lastly, it is met with in patients who have died from phosphorus or arsenic poisoning, or in a minor degree from alcohol, antimony, and sulphuric ether poisoning (§ 110,

p. 82). In some few cases, fatty degeneration is found to be due to the partial occlusion of the coronary arteries, brought about by the process of endarteritis deformans, in connection with a similar condition in the aorta, or by some other obstructive lesion. It also occurs as a sequel to endocarditis and pericarditis.

To the naked eye the heart has a certain characteristic appearance. It is somewhat dilated, and on the endocardial surface the muscle is seen to be considerably paler than normal, and on section it has the same pale smooth appearance, especially towards the endocardial surface. As a rule, this pallor is not equally diffused over the whole surface, but appears to be more marked in certain patches, affecting specially the musculi papillares and columni carnæ.

On examining one of the musculi papillares, taking it as a typical specimen of an affected part, it is found that there are numerous small, dark, cream-coloured areas, which stand out pretty prominently and fairly well defined from the reddish brown background. This has been very aptly compared to a "thrush's breast," and also to "faded leaves." In very advanced cases the cream-coloured patches have spread so far as to meet one another, in which case the "thrush's breast" simile does not hold good. Where this form of degeneration is due to phosphorus or arsenic poisoning, scarlet fever, or leucocythemia, small hæmorrhages may be met with immediately beneath the pericardium. The muscular tissue is flabby and somewhat, or in some cases very, friable, so much so, that the thumb and fingers are very readily made to meet through the muscular wall.

Harden a piece of the heart in Müller's fluid (§ 53, p. 42)—not spirit—cut sections (§ 67, p. 48), mount one unstained in normal solution (§ 34, p. 32), stain one with osmic acid (§ 80, p. 62), and another in picro-carmine (§ 73, p. 53), both of which must be mounted in Farrant's solution (§ 98, p. 71). Have several sections ready on which to act with various reagents, which will be afterwards mentioned.

On examining a section under the low power (× 50) very little is to be discerned beyond the fact that the muscular fibres appear in some cases to have become slightly enlarged. This is especially the case where the fatty degeneration follows upon an inflammatory condition; but in the pure degeneration, such as that brought about by metallic poisoning, the fibres are never increased in size. The

enlargement of the fibres can never be definitely made out if it is not remembered that as the fibres increase in size the spaces between them become somewhat narrower, and the contained tissue elements crowded together.

In a picro-carmine stained specimen, or in a specimen stained with eosine and logwood (§ 79, p. 62), and mounted in Canada balsam (§ 96, p. 69), the nuclei between the muscle fibres are sometimes increased in number and distinctness. Find a thin part, and then examine under a high power (× 300 or 400), which is obtained by pulling out the draw-tube of the microscope to the fullest extent. The transverse striation will be found to have to a great extent disappeared. In some fibres not a trace of it is left, whilst in the fibres in which the change is not so far advanced the striation is seen only at the margins of the cells. In such cases, where the centre of the cell chiefly is affected, the transverse striation is replaced by a number of small round granules, or in some cases globules, which never,

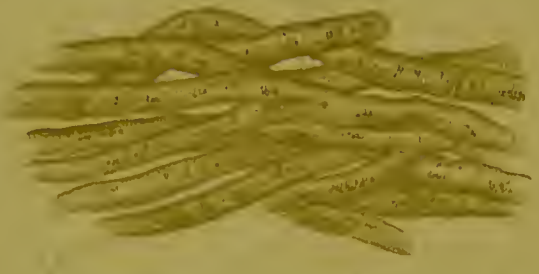


FIG. 36.—Muscular fibres of the heart. Fatty degeneration. Mounted unstained in Farrant's solution. (× 300.)

f. Muscular fibre in which there is slight dimming of the transverse striation.

f.c. Small fatty granules and globules along the lines of longitudinal striation, especially around the nuclei and near the centres of the cells.

however, reach even a medium size,—all remaining extremely small. They first make their appearance at the poles of the muscle corpuscles (the oval mass of protoplasm with its nucleus in the centre). From these points the process gradually extends through the length of the fibre, until eventually the whole of it is involved. The fibre then appears to be made up of a series of rows of small round granules and globules, each row corresponding more or less to one of the fibrillæ of which the fibre is made up, so that at this stage the fibre, though perfectly well defined, has lost its transverse striation, and appears to

be made up of rows of small, highly refractile bodies (like so many strings of beads). This condition resembles to a certain extent that seen in cloudy swelling, but may be distinguished from it in the following respects: the granules and globules are obscure and somewhat larger, and, in the section stained with osmic acid, are black or brownish black, which is not the case with the granules in cloudy swelling. On the other hand, the fattily degenerated muscle is quite unaffected when a drop of acetic acid is run under the cover glass from its margin. Treated with chloroform, ether, &c., the fatty material is dissolved, whilst the granules of cloudy swelling are unaffected. The transverse striation in this condition may be almost lost. As already noticed, the fatty degeneration occurs in localised patches, and as the section is examined under this high power, the same fibres may be fatty in parts, whilst in other parts they are to all intents and purposes healthy. With the microscope these areas can be localised much more accurately than with the naked eye.

Fatty infiltration is frequently associated with fatty degeneration. In fact, as already pointed out, the infiltration when extensive may so compress the muscular fibres as to interfere very seriously with their nutrition and function, and so bring about the degenerative change in their substance.

Pigmentary Degeneration, or Brown Atrophy of the Heart.

135. This is a condition met with most frequently in cases of general disease, where the process of exhaustion has been long continued. Consequently it is often found associated with fatty degeneration of the muscle in such conditions as phthisis, or more markedly still in Addison's disease. The pure brown atrophy is more frequently met with in the hearts of old people; but marked pigmentation may be present in any hypertrophied heart.

The naked eye appearances vary somewhat in different cases. When it is found in connection with atrophic conditions, the heart is considerably smaller, the walls are thinner, the cavities appear to be contracted, the coronary arteries are tortuous and appear to be larger than normal. The pericardium is frequently thrown into folds, and is dark brown in colour. If the condition is unaccompanied by fatty degeneration, the muscle may be firm or even tough; but when asso-

ciated with that condition, it is friable and soft, in which case, too, there are paler patches embedded in the dark brown background. Where it occurs along with hypertrophy, the colour is not so dark, the tissue is firmer, and it may be that none of the characteristic features seen in the above form are present.

For microscopic examination, prepare in Müller's fluid (§ 53, p. 42), cut (§ 67, p. 48), mount a section unstained and another stained with picro-carmine (§ 73, p. 53), both in Farrant's solution (§ 98, p. 71). A section taken from a heart removed from a patient affected with Addison's disease is perhaps the best for examination.

Examine the unstained specimen under a low power (× 50). The fibres will be seen to be thinner than normal, as they are evidently not so closely packed as in the healthy heart. It will be noticed, too, that the fibres are considerably broken up, the constituent muscle elements or muscle cells, with their serrated ends, being separated by intervals more or less marked in different places. In these muscle elements, situated at about their centre, a dark brown spot can generally be made out even under this power; and if a bundle of fibres is examined in transverse section, a similar dark spot may be made out in most of the fibres occupying the centre of the section.

Examine under a high power (× 400). Where the pigmentary degeneration is unaccompanied by fatty degeneration, the transverse striation of the fibres is extremely well marked. Examine the short segments into which the fibres are divided, and note that the ends are serrated. In the centre of the segment the largest mass of pigment is observed occupying the position of the muscle corpuscle around which it is collected, especially towards the poles. In relation to this it will be remembered that even in the normal heart there is a small quantity of golden brown pigment collected at each pole of the muscle corpuscle. So far, then, there is simply an exaggeration of a normal process. Where the condition is advanced, as in the section now under observation, it will be found that the pigment appears in elongated patches, following more or less regularly the lines of longitudinal striation. These patches are not confined to any part of the muscle element, but are more frequently seen at some distance from the periphery than near the margins. The granules of which the patches are composed vary slightly in size, but all alike are of a beautiful

golden yellow colour, when seen under a high power and by a strong light. In a transverse section of one of the muscular fibres the pigment is seen as a golden yellow mass, occupying the centre of the section of the fibre, whilst the smaller masses appear as minute points of the

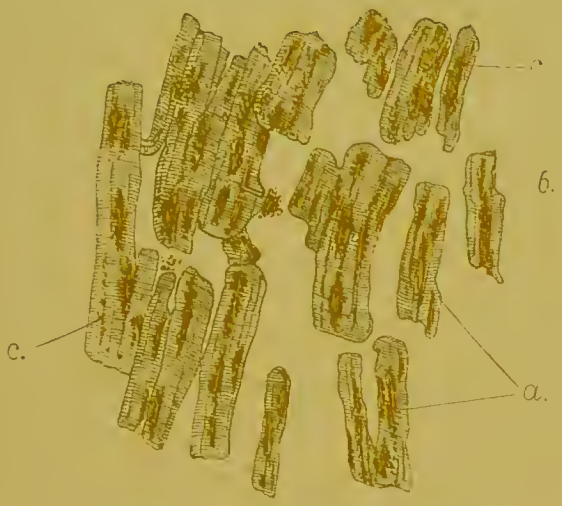


FIG. 37.—Brown atrophy of the heart. Muscular fibres broken up into short segments. Mounted unstained in Farrant's solution. (× 400.)

a. Fibres splitting up into short detached fragments.
b. Pigment collected around the nucleus.
c.c. Pigment scattered along lines of longitudinal striation.
It will be noted that the transverse striation is very distinctly marked in this condition.

colour scattered throughout the substance of the fibre. In the picro-carmine stained specimen the nuclei may in some few instances be seen as pink-stained bodies; but in the majority of the fibres the accumulation of pigment is so great that the nucleus is completely obscured.

The pigment is some altered form of hæmoglobin; but whether there is any accession from the blood, or whether there is simply a concentration of that which already existed in the muscle, is as yet merely a matter for conjecture.

ACUTE MYOCARDITIS.

136. Having considered the above conditions, a few words still remain to be said about certain appearances which are frequently associated with one or other of the above forms of disease of the muscular walls of the heart. First, as to myocarditis, which may occur either as a primary or secondary change, but which is found to occur much more frequently

as the latter. In such a case it extends from the pericardial or endocardial surface into the substance of the muscle proper, or along the course of the connective tissue framework which supports the bands of muscular tissue. Take a couple of sections from a heart in which there is acute myocarditis, the presence of which is suggested by the symptoms during life, and after death by the racemose reddening of the endocardium, the friability, along with the deepened colour, and the yellow patches on, or mottling of, the muscular wall. Stain one of the sections in picro-carmine (§ 72, p. 53), and mount in Farrant's solution (§ 98, p. 71); the second in logwood (§ 74, p. 57), and mount in Canada balsam (§ 96, p. 69).

Examined under the low power (× 50), the fibres are seen to be swollen and closely packed together. If the disease has been very acute, small areas of extremely opaque bluish grey looking material (in some cases pink) may be seen scattered over the yellow muscular tissue; between the individual fibres or around the smaller vessels a vast number of very small pink points are seen. (In the logwood stained section these come out more distinctly as blue points.)

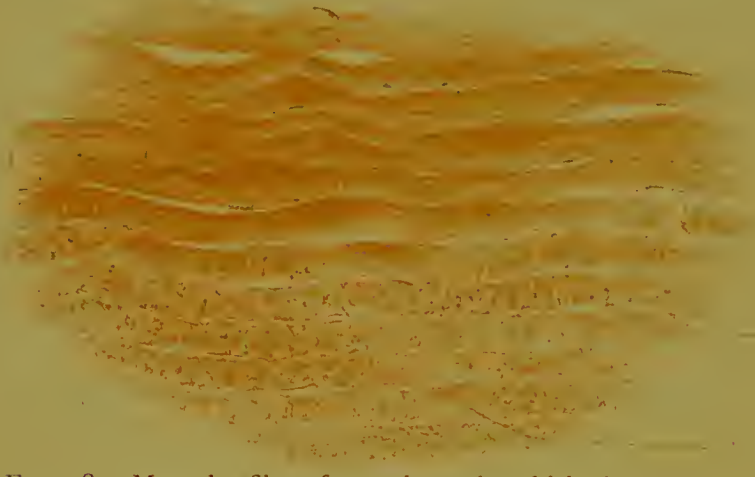


FIG. 38.—Muscular fibres from a heart in which there was acute endocarditis, stained with picro-carmine, and mounted in Farrant's solution. (× 300.)

a. Fibres comparatively healthy in a condition of cloudy swelling.

b. Fibres broken down into an almost granular mass. These fibres are slightly but irregularly swollen.

c. Parts of the fibres as yet only in the condition of cloudy swelling. These are placed between parts which are in the more advanced stage of disintegration.

Examine under the high power (× 400). The bluish grey areas are composed of swollen and bulging fibres which have lost all trace

of striation, and present the appearance of broken down glassy looking protoplasm, having in some parts almost angular depressions and bulgings (the so-called vitreous degeneration), or the muscular fibres have become broken down, and there is simply a mass of more or less granular *débris*. These are evidently the fibres in which the degenerative process is taking place most rapidly; some of the yellower looking fibres appear quite normal, whilst others are in an advanced state of cloudy swelling (§ 132, p. 133). The nuclei of the connective tissue spaces are considerably increased in number, most of the pink nuclei lying around the vessels from which they have probably emigrated. Some of the nuclei, however, are derived from the connective tissue corpuscles, which in this condition are more highly nourished and undergo rapid proliferation. The vessels are, as a rule, somewhat dilated. On staining a section with osmic acid (§ 80, p. 62), not a single black granule can be distinguished, showing that, as yet, fatty degeneration has not set in. If the condition is not quite so acute, and the patient survives rather longer, the black reaction with the osmic acid is given at some points in the mass of *débris*, which is now much more granular.

Chronic Myocarditis.

137. In the more chronic form of myocarditis, which is rather an interstitial inflammation than a true inflammation of the muscle, the principal change in the first instance is an enormous proliferation of the connective tissue corpuscles, which can be seen under the low power of the microscope as lines, or accumulations of deeply stained bodies, following pretty closely the lines of the vessels. In some cases these nuclei form bands almost as broad as the bands of muscular tissue. The smaller vessels are often increased in size, and their walls undergo a considerable amount of thickening, especially in the adventitia.

Under the high power (× 400), the muscular fibres may be perfectly normal in appearance, but between them the deeply stained nuclei are very numerous, and the dilated blood-vessels with their thickened walls are also well seen, the thickening being due chiefly to an increase in the number of cells in the adventitia. Where the condition is more chronic still, or where the patient (say in acute

rheumatism) pulls through this period, the young cells become organised into fibrous tissue, which stains pink with picro-carmine, and in which are seen a number of connective tissue cells appearing somewhat spindle-shaped, as they are most frequently seen in section. Where this stage is reached, the muscular fibres are usually undergoing atrophy or fatty degeneration, though neither of them is by any means invariably met with. When it does occur, the fatty change appears to be due to malnutrition of the fibres, brought about, first, by the condition of the blood which has caused the fibrous increase, and, second, by the mechanical pressure of the newly-formed fibrous tissue on the muscular fibres. The fatty fibres are similar in appearance to those previously described (§ 134, p. 138). A condition spoken of as cardiac sclerosis is described by Cornil and Ranvier, in which the essential details are similar to the above. It occurs very frequently during the course of interstitial nephritis, more especially in patients who are at the same time suffering from maniacal symptoms.

In a heart in which there is aneurism at the apex of the left ventricle (by far the commonest position), the muscular fibre is generally found to be in a state of fatty degeneration, though in some cases the myocardium and the endocardium show evidences of acute inflammatory processes. Even in the aneurisms at the base of the heart in the interventricular septum, which are continuations of valvular aneurisms, the muscular fibres in the immediate neighbourhood usually undergo fatty degeneration.

Endocarditis.

138. An examination of three specimens of this condition will be sufficient for all practical purposes. The structure of the endocardium has been already briefly described (§ 131, p. 132). The results of endocarditis are most frequently evident in connection with the valves of the various orifices, and it will be as well to see what parts of the endocardium enter into the structure of the valves, and their relative proportions. The layer of flattened connective tissue cells, with the fibrillated tissue and yellow elastic fibres, which has already been described as lying immediately under the layer of endothelium, is con-

tinuous from both the auricles and the ventricles on to their respective valves. The endothelial covering is also continuous, and is further prolonged over the chordæ tendiniæ, which are composed of the yellow elastic and white fibrous tissues, so that any process affecting the surfaces of the valves is most frequently continued along the chordæ tendiniæ. The aortic and pulmonary valves are in the same manner covered with a layer of endothelium, that of the heart becoming continuous with that of the vessel, and the subjacent condensed layer of fibro-elastic tissue of the one becoming continuous at the margin of the valve with that of the other.

Acute Endocarditis.

139. Acute endocarditis is met with in patients who have succumbed to acute rheumatism during the early stages of the disease. The most marked evidences of the disease are in the form of verrucous growths, which make their appearance along the lines of contact of the valves, chiefly in the left side of the heart, the mitral and aortic valves consequently being specially affected—the former on the auricular aspect near the margins, and the latter on the ventricular aspect, also at some little distance from the margins of the cusps. These warty growths are much more rarely met with on the tricuspid and pulmonary valves, but when they do occur the same rules as to position hold good. The growth or vegetation appears to be "soft, friable, and semi-transparent." In the more acute form it never reaches any very great size, but similar small growths occur all along the points of contact of the valves. If separated from the valve, a small portion of the subjacent tissue is brought away, leaving an ulcer the size of the base of the vegetation. If the patient has survived the early stages of the disease, the growths may increase considerably in size, but they have much the same structure as the smaller forms. Along with these vegetations, at the points of contact with the valves, others may occur on the whole of the auricular surfaces of the valves, but the process radiates from the primary focus. The chordæ tendiniæ, which, as already observed, are simply continuations of the endocardial covering of the valves, are very much swollen and extremely brittle.

To examine such a valve microscopically, a piece of it, on which is a good vegetation, should be cut out and hardened in absolute alcohol (§ 51, p. 42), and a second piece in Müller's fluid (§ 53, p. 42). Cut sections (§ 67, p. 48) through the vegetation and the valve at right angles to the plane of the valve. Stain a section in logwood (§ 74, p. 57), and mount in Canada balsam (§ 96, p. 69). Stain a second in picro-carmine (§ 73, p. 53), and mount in Farrant's solution (§ 98, p. 71). If it is intended to search for the micrococci on the surface of the vegetation, the preparation hardened in absolute alcohol must be cut and sections of it stained in methylaniline violet (§ 76, p. 59) and mounted in Farrant's solution or Canada balsam.

On examining a section with the low power (× 50) the base of the growth appears to be made up of a great number of small round cells, which are deeply stained with most of the reagents that may be used. This mass of small round cells is continuous with a similar layer found infiltrating the endocardium in the neighbourhood of the growth; on the surface of this mass of granulation tissue (for it is nothing more nor less than this) is found some granular looking *débris*, which with picro-carmine takes on a yellow colour (or in some parts pink); and scattered through it are a few pink-stained cells, whilst further out still is a very thin layer of fibrin, which is usually granular and somewhat opaque, and stains a pinkish colour with picro-carmine.

If the section be stained with methylaniline violet, a deeper colour may be observed near the surface of the vegetation, even under the low power.

High power (× 300).—Under this power the cells of the endocardial tissue are seen to have undergone very rapid proliferation, and it is from this source that the tissue composing the greater part of the growth arises; the proliferation is so rapid and so great, that, just as in the case of a granulating wound, the mass of cells passes beyond the level of the endocardium, and a small projection is the result. The yellowish mass on the surface is made up of two factors, degenerating cells and coagulated fibrin, both of which may be readily distinguished by the picro-carmine and other staining methods.

In a section stained with methylaniline violet (§ 76, p. 59) and mounted in Canada balsam (§ 96, p. 69), a number of micrococci may be seen, forming a deeply stained granular layer on the surface

of the disintegrating cells and fibrin. In the ordinary acute endocarditis these micrococci do not appear to give rise to any serious changes, even when they are carried off along with parts of the degenerating mass near the surface to form minute embolic infarcts in some organ. Chemically, they appear to be comparatively inert.

Chronic Endocarditis.

140. As with all inflammatory processes, acute endocarditis tends to become chronic—especially if not extremely acute at the commencement—in which case the following very characteristic appearances are presented to the naked eye. The vegetations in the positions already mentioned are now firm, hard, fibroid masses, have a broad base, and are not so prominent as in the acute form. The edges of the valve are frequently thickened, and the thickening is especially well marked along the lines of contact. At certain points the thickened valves have become bound together by the organisation of the inflammatory products, and they are found to be puckered and retracted. As in the case of acute endocarditis, the changes take place principally in the valves of the left side of the heart, and on the auricular surface of the mitral valve, and the ventricular surface of the aortic valve. In some few cases the thickening extends in both directions, so that the walls of the cavities as well as the valves are affected. The chordæ tendiniæ are shortened, thickened, opaque looking, and present almost the appearances of pieces of firm cartilage. In place of being brittle, as in the acute form, they are extremely tough. In the mass of thickened fibroid tissue, calcareous plates may be frequently observed immediately under the endothelial covering, or pultaceous or fatty granular material may occupy the same position.

Harden one of the valves, on which is one of the flattened vegetations, in Müller's fluid (§ 53, p. 42), and put a second, with some of the fatty and calcareous patches, to harden in the same manner.

Make sections (§ 67, p. 48), stain one in picro-carmine (§ 73, p. 53), and mount in Farrant's solution (§ 98, p. 71); a second in logwood (§ 74, p. 56), and mount in Canada balsam (§ 96, p. 69).

Examine the first of these under a low power (× 50). In place of the round cells which were observed in the acute vegetation, and in

the endocardium beneath it, there are now a number of spindle-shaped (as seen in section) cells, the nuclei of which are more or less deeply stained with carmine. Between these flattened cells (for flattened branched cells they will be found to be if examined from the surface) are layers of fibrillar substance arranged in regular lamellæ, giving rise to the appearance of a very much thickened endocardium. This lamellated tissue is stained a delicate pink with picro-carmine, and gives all the reactions of fibrous tissue. On the surface of the vegetation there is frequently a deposition of fibrin, but it is usually freshly deposited, and does not stain, although a few cells entangled in the fibrinous meshes are deeply stained. This fibrin has therefore been deposited whilst the blood current was slowing, and as the patient was dying. In fact, in almost all sections of vegetations examined, if there is a deposit of fibrin on the surface, the greater part of it has been deposited during the last few days of the patient's life.

Examine the section in which the fatty and calcareous plates were seen (× 300). In the spaces originally occupied by the flattened cells, there is now most frequently a mass of yellow-stained granular material. In the deeper endocardial layer this granular material is replaced by a number of highly refractile granules, which, on the addition of a drop of hydrochloric acid, evolve bubbles of gas (carbon dioxide), and then disappear. These highly refractile granules are small calcareous particles deposited in the fatty material. In some few places the fibrous tissue is also undergoing the fatty degeneration and calcareous infiltration, so that large calcareous patches may be formed. In the very early stages, however, the change is confined to the spaces in which the flattened cells lie, and the intercellular fibrous tissue is stained a beautiful pink. This condition should be studied along with endarteritis deformans, to which it bears a very close resemblance (§ 148, p. 159), especially in the more chronic forms in old people, when it occurs on the aortic surface of the semilunar valve. Compare the vegetation in the early stages with a mass of granulation tissue, growing on a free surface, that of an ulcer, for example. In the later stages the vegetation may be likened to the fibrous cicatrix which is left when the ulcer has healed. If such tissues are examined together, it will at once be seen how closely the two stages of the one correspond to the two stages of the other.

Acute Ulcerative Endocarditis.

141. This condition, which in many respects resembles the acute form of endocarditis already examined and is by many writers considered to be the same disease, differs from it apparently in the two following points :—*1st*, That its local action is more destructive ; and *2nd*, That the fragments detached and carried into the circulation give rise to a much more rapid and widespread mischief than do emboli from the simple acute form. To the naked eye the vegetations appear to be very similar to those described in the simple form, but they tend to occur more indiscriminately over the endocardial surface of the valves or of the heart wall. They also appear to be much more liable to break down and leave ulcerated patches. The vegetation itself (taken, for example, from a case of ulcerative endocarditis occurring during the course of a case of pyæmia), if stained and examined as in the acute form, will be found to present exactly the same character under both low and high powers, as already described (§ 139, p. 146), the micrococci in the superficial layer being especially well seen. Harden in absolute alcohol (§ 51, p. 42) a piece of a valve on which is one of the ulcerations. Stain a section with osmic acid (§ 80, p. 62), a second in picro-carmine (§ 73, p. 53); and mount both in Farrant's solution (§ 98, p. 71).

Examine under the low power (× 50). The floor and margins of the ulcer are infiltrated with a great number of small round cells, which take on the carmine very well, except at the surface, where there is a distinct yellowish tinge, which points to the fact that the tissues are here undergoing degenerative changes. In the section stained with osmic acid this same area appears to be much darker in colour than the deeper tissue.

Examine under the high power (× 300). The pink-stained cells are very readily discerned closely packed together, forming the floor and margins of the slight depressions or even roughened elevation. Directly in contact with the blood, however, is a layer of extremely granular looking cells, the granules in some cases appearing almost like small globules. This layer is stained more or less yellow with the picro-carmine, and the small globules (which are often free)

and granules are stained black with osmic acid. Here, too, small quantities of free blood-pigment may be observed. Mixed up with this layer of degenerated tissue is frequently a quantity of granular looking fibrin, in which, in a section stained with methylaniline violet (§ 76, p. 59), may be seen colonies of micrococci, some of these colonies being of considerable size.

Pericarditis (Simple, Purulent, and Tubercular).

(*See Chapter on Lung.*)

142. The conditions under which pericarditis occurs, its naked eye and microscopic appearances, are very similar to the conditions and appearances of pleurisy, and as it is desirable to repeat as little as possible in a work of this character, the student is referred to the chapter on the Lung and Pleura for the description of inflammation of a serous surface. The two conditions are identical, and to understand one is to understand both.

Tumours met with in the Heart.

Tubercle in pericardium (rarely in other tissues), syphilitic gummata, secondary cancers and sarcomas (rarely primary), fibroma, myxoma, and lipoma.

Cystic Parasites.

Hydatids of *Tænia echinococcus*, and cysticercus cellulosæ of *Tænia solium*.

CHAPTER V.

BLOOD-VESSELS.

Normal Histology.

143. Capillary vessels consist simply of a single layer of more or less flattened endothelial cells. Each cell contains a flattened nucleus, by which the capillary vessel is most easily recognised. Between the cells is a cement substance, which is stained brown with nitrate of silver. The cement substance is supposed to have considerable pathological importance, as, in the process of inflammation, where the vessels are distended, and the cement substance gives way, open-



Fig. 39.—Drawing of capillary vessel, with surrounding adenoid tissue. (× 300, after Klein and Noble.)

a. Nucleus of flattened endothelial cell, forming the inner layer of the vessel.

b. Flattened cells (really connective tissue cells) surrounding capillary (perithelium).

c. Lymphoid cells in meshes of the network.

ings are said to make their appearance, through which the coloured and colourless blood corpuscles find their way from the vessel.

Around some of the capillaries there is a second sheath, sometimes spoken of as the perithelium, which is composed of "a network of branched connective tissue cells." This is also of great pathological importance, as it is in fibrils on which these rest that the process of waxy degeneration is supposed to occur.

144. A medium sized artery is made up of three layers or coats—the "intima," the "media," and the "adventitia."

The tunica intima is composed (1.) of a layer of endothelial cells, very similar in appearance to those already described in the capillaries; (2.) subendothelial connective tissue or intima proper, which consists of longitudinal and transverse laminated tissue with branching connective tissue cells lying between; (3.) the so-called internal elastic

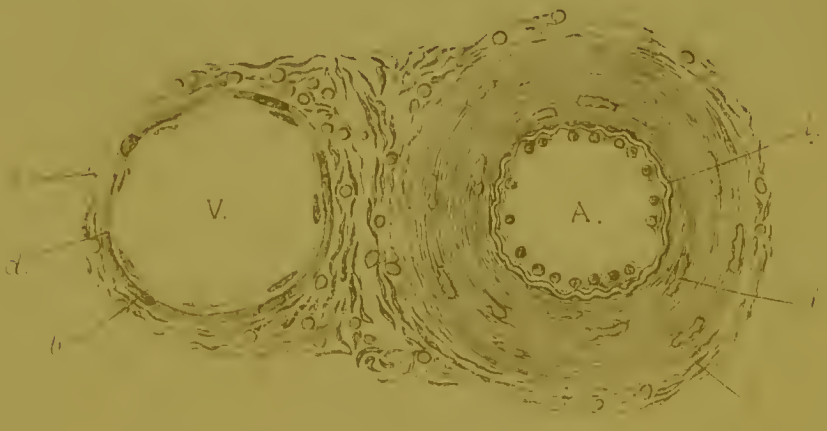


FIG. 40.—Transverse section of normal artery and vein. (× 350, after Klein and Noble Smith.)

A. Artery, with (*a.*) lining nucleated endothelium.
b. Internal elastic lamina thrown into folds by the contraction of
d. The thick muscular coat, composed of non-striped muscular fibres, the nuclei of which are seen as deeply stained rod-shaped nuclei.
c. Fibro-cellular adventitia.
V. Vein, with (*a.*) flattened endothelial cells.
b. Thin intima.
d. Thin muscular coat.
c. Fibro-cellular adventitia.

lamina, an elastic homogeneous layer, which is, as a rule, wavy when the vessel has been hardened. It is composed of interlacing bands

of elastic tissue, between which are openings; through these the vessels of the media may make their way during the process of organisation in a blood-clot.

The media or muscular coat is composed of non-striped muscular fibres, arranged principally transversely to the axis of the vessels. Where more than one layer is present, they are arranged regularly, and rod-shaped nuclei may be seen in the fibres. Between the individual layers laminæ and networks of elastic tissue are found, and in the larger branches these elastic laminæ are especially prominent. Vasa vasorum are found passing from the adventitia for some distance into the substance of the media, the capillaries of these vessels stopping short at the part of the coat next the intima, which rarely receives capillaries from this source. In the smaller vessels the adventitia is in direct contact with the media, but in the larger arteries there is an elastic network separating the two coats. This is spoken of as the external elastic lamina.

The adventitia is composed of connective tissue, with numerous cells, between which are bundles of pink-stained (with picro-carmine) fibrous tissue, with here and there, especially near the media, longitudinal bundles of yellow elastic fibres. With the same staining fluid the elastic laminæ are stained yellow. Small vessels invariably run into the adventitia to supply the walls of the vessels with nutriment.

145. The aorta differs somewhat from the above. The adventitia is comparatively thin, the media has relatively little muscular tissue in its composition, the internal elastic lamina of the smaller vessels being apparently represented by a number of thin layers of elastic tissue interspersed through the muscular tissue, networks of elastic and connective tissue running along with the vasa vasorum. Here, too, the intima is thicker than in any other vessel. It is composed of a thickened subendothelial layer, in which are numerous flattened nucleated connective tissue corpuscles, with a layer of more or less reticulated elastic tissue beneath.

The veins have the same coats as the arteries, but the chief characteristics are, that the adventitia is the most prominent coat; the media is composed of irregular bundles of non-striped muscular fibre, with little or no elastic tissue, but simply a basis of connective tissue;

the various structures of the intima are here much more delicate. The valves are formed of folds of the intima, in which a portion of the muscular coat is invaginated.

In all vessels there are numerous lymphatics (spaces lined with endothelium) found in the adventitia, and in the larger vessels tubular lymphatics in the same position. Lymph spaces between the bundles of muscular tissue are also met with, which communicate with the lymphatics of the adventitia.

Acute Endarteritis.

146. This form of inflammation is met with principally in the aorta, but it may also occur in the smaller vessels, especially in those near wounds. The appearances to the naked eye are very characteristic. On the inner surface of the aorta are one or more patches of soft elastic or gelatinous looking material of a yellowish, or, it may be, of a pearly pink colour. The patches vary in size, but are generally from a quarter of an inch to half an inch in diameter, and are sharply defined from the surrounding intima, which is almost normal, or only slightly swollen, and thrown into small folds, in the immediate neighbourhood of the swelling. It is, as already stated, met with most frequently in the aorta, and in the first part of the aorta, especially near the coronary arteries. On examining the outer surface of the vessel it is found to be in a state of inflammation, and a mass of semi-gelatinous or œdematous looking tissue, having a pink tinge, is seen, from which it is evident that this acute endarteritis is accompanied by periarteritis. In some cases the media is also swollen and infiltrated looking.

Preserve a part of the aorta with one of these patches in Müller's fluid (§ 53, p. 42), cut sections transversely to the long axis, stain a section in picro-carmine (§ 73, p. 53), and mount in Farrant's solution (§ 98, p. 71).

Examine under a low power (× 50). The cells of the intima are undergoing rapid proliferation, they are extremely numerous, and are separated only by thin layers of the laminated tissue. Where the thickening is considerable, these rounded cells are exceedingly numerous. Where the thickening is as yet not very well marked,

there are in the deeper layers flattened cells with somewhat elongated nuclei still to be seen. All these cells are stained deeply with the carmine of the picro-carmine.

Where the condition is advanced, there is also a marked increase in the number of cells in the adventitia; the increase in some cases becoming so great that the adventitia looks more like a mass of granulation tissue than anything else. In some few cases, small round cells, deeply stained with carmine, may be seen scattered through the yellower muscular tissue, but, as a rule, the middle coat is unaffected.

Under the high power (× 300) the cells in the superficial part of the intima must now be examined. They are composed of nuclei, surrounded by thin films of protoplasm, and all give evidence of great vegetative activity. Their growth is maintained at the expense of the fibrous laminæ. In the deeper layers, or where the process is not so far advanced, the flattened nucleated cells are still seen, but they are becoming cloudy and granular. In the adventitia the capillary vessels are becoming more prominent and distended, whilst new loops are frequently sent through the media into the thickened intima. Along the course of the vessels, which may be seen as double rows of flattened connective tissue (endothelioid) cells, are numerous small round cells, some composed of little but a nucleus, others having around the nucleus a quantity of protoplasm. As these cells are developed, and the connective tissue fibrils are absorbed, the wall of the vessel may become considerably weakened; where these patches occur in the very acute form, aneurisms may result from the wall of the vessel giving way at the weakened point. (*Acute Multiple Aneurisms.*)

As in all cases where there is a formation of granulation tissue, the process may become more chronic, in which case there is a formation of fibrous tissue. This takes place especially around the mouths of the branches of the aorta,—*e.g.*, in the coronary arteries, the mouths of which are frequently surrounded by constricting bands of fibrous tissue, formed by the organisation of the round-celled tissue, as the process has become more chronic.

Chronic Endarteritis—"Endarteritis Deformans"—"Atheroma."

147. It will perhaps be well to describe this change first as occurring in one of the smaller vessels, and then in the aorta. . It occurs especially in the vessels of aged people, and is to be looked upon as a degenerative inflammatory process. In the vessel from which the section below described was taken, there were patches of opaque, pale, firm tissue; in some places quite hard and gritty when cut, scattered at irregular intervals along the course of the vessels (taken from the base of the brain).

These patches vary from one-sixth of an inch to one-third of an inch in length, and are generally confined to one side of the vessel, so that on section the vessel wall is seen to be much thicker on one side of the lumen than on the other. On cutting into these masses, they are found to be firm, hard, and in many cases calcareous and gritty feeling, some of them "cutting" almost like cartilage or fibrous tissue, or, frequently softened and yellow in the centre. The lumen is very much narrowed in places, whilst the vessel is completely blocked at one part by a clot of blood which has become adherent to the thickened and roughened wall.

Harden in Müller's fluid (§ 53, p. 42) or spirit (§ 52, p. 42), stain a section in picro-carmine (§ 73, p. 53), and mount in Farrant's solution (§ 98, p. 71). Stain a second in logwood (§ 74, p. 57), and mount in Canada balsam (§ 96, p. 69).

Low power (× 50).—It is at once observed that the wall of the vessel is very unequally affected. First find the internal elastic lamina, which may be recognised as a wavy yellow line (with picro-carmine) situated immediately within the muscular layer (known by its regular lamination and the rod-shaped nuclei). The change takes place almost entirely within the internal elastic lamina, but is very unequally distributed on the wall of the vessel, so that on examination in section the vessel has somewhat the appearance of a signet-ring.

At the point where least change is seen, there is simply a thickening of the laminated part of the intima, accompanied by a proliferation of the flattened cells which lie between the fibrous laminæ. The endothelium does not appear to have proliferated; from this point

the thickening gradually increases until it is very marked, involving about half the circumference of the vessel. Where it is most marked, the intima appears to split into two layers, each of which is composed of laminated, fibrous-looking tissue, whilst between the two laminæ is seen an open space. It will perhaps be advisable to examine the different layers, from the lumen to the intima, in order.

Near the lumen the fibrous tissue, as in the thinner part, is stained pink, showing occasionally the nucleus of a flattened cell. The cells in this position are increased in size and take on the staining somewhat deeply.

Beneath this layer comes a mass of similar flattened laminated tissue, but the spaces in which the cells lie are much larger, and the cells are very granular in appearance and do not completely fill the spaces. In the deeper part of the layer, these spaces apparently run into one another, and are filled with a bluish grey, highly refractile material, which disappears on the addition of hydrochloric acid with the evolution of carbon dioxide. After this comes a mass of homogeneous looking material, stained unequally a dirty pink, in which are numerous irregular slits or openings running in all directions; and in the openings are granular or semi-crystalline bodies which are identical in appearance with those in the more regular openings. Some of the irregular openings are of considerable size, and contain granular *débris* in addition to the bluish grey material. In most cases the internal elastic lamina marks out sharply the diseased from the healthy tissues; but in the more advanced condition the bounding lamina has given way, and a process similar to that described in the deeper layers may be observed in the muscular media, the muscular layer apparently becoming broken down and atrophied.

In a logwood-stained specimen very similar details come out, but the nuclei near the lumen appear much more prominent than do those in the deeper layers.

Examine under the high power (× 300) immediately under the endothelium, where the earliest indications of the advancing change can be made out. The laminæ which were so distinctly seen under the low power are now seen to be separated from one another, and the intervals are occupied by a number of cells, which, near the surface, are numerous, rounded, and deeply stained, lying in rows



FIG. 41.—Section of medium sized vessel (cerebral artery), endarteritis deformans, stained with picro-carmine. (× 250.)

a. Placed in the lumen of the vessel.
b. Small round cells immediately under layer of endothelium.
c. Thickened intima, with flattened laminæ and flat cells (corneal structure), cells and laminæ both swollen.
d. Region in which cells and intercellular laminæ are both becoming granular and swollen (fatty and calcareous deposit).
e. Broken-down tissue, in which are large cracks and fissures, calcareous salts, crystals, &c.
f. Layer next to internal elastic lamina, similar in appearance and structure to *d*.
g. Yellow internal elastic lamina.
h. Muscular media, perfectly healthy.

between the separated laminæ. Some of them are composed of nuclei only, others are undergoing swelling and proliferation, whilst others again are surrounded by a thin film of protoplasm. The laminæ in this position are also swollen. As the distance from the surface increases, the proportion of cells to fibres diminishes, the cells become flattened, not so deeply stained, and in many cases granular, this material becoming more marked further from the surface, the granules stain black with osmic acid in the deeper parts. Later, a number of similar granules make their appearance in the swollen fibrous tissue. The spaces around the granular material are very much enlarged, as though they had at some time been distended; but now they contain only the *débris* of such tissue as had originally caused distention. When cells and matrix have both become granular, the whole mass may break down, and the large spaces containing the calcareous looking material (some parts of it being granular, others crystalline) are seen. In some of the spaces or cavities a few crystals of cholesterin may be met with, recognised by the fact that when a section is stained with iodine and then transferred to a weak solution of sulphuric acid (§ 78, p. 62), the crystal is stained blue, especially at the edges.

Where the calcification has passed into the middle coat, the appearance

presented is exactly that which is seen in the deeper layer of the intima—a homogeneous or granular matrix, in which are numerous large spaces containing the granular *débris* and highly refractile crystals. This is usually accompanied by an increase in the number of cells in the adventitia, pointing to the fact that there is now a condition of periarteritis.

The principal points to be noticed are, that part only of the circumference of the wall of the vessel is affected, that the change takes place in the subendothelial tissue, commencing as a swelling and proliferation of the cells, followed immediately by a swelling of the fibrous matrix. These in turn undergo fatty degeneration and calcareous infiltration in the same order, the most marked changes taking place in the deepest layers of the swollen and proliferating tissue, the earliest changes being always noticed near the lumen of the vessel. As a rule, the internal elastic lamina sharply defines the diseased area, but this is not always the case; and when the media is invaded, the adventitia very frequently becomes secondarily affected.

Atheroma of the Aorta (Endarteritis Deformans).

148. *Naked eye appearances.*—It is most frequently met with in the first part of the aorta, where also it is seen in the most advanced stage, but it may occur in any part of the vessel, and is common around the openings of its branches, especially about the orifices of those branches springing from the arch, and then around the other vessels, in regular order from above downwards. It appears to affect those parts of the aorta at which the strain is greatest, and the movement most continuous. It may, for the sake of convenience, be divided into four stages, but all the four stages may be observed in the same vessel. The earliest change takes the form of a pale, opaque, translucent or opalescent, somewhat gelatinous looking swelling of the intima. These swellings vary considerably in size, but are seldom more than half an inch in diameter; they are rounded or oval, and the surface is perfectly smooth, so that they are evidently beneath the endothelium which lines the vessel. In some cases these rounded patches are so near together that as they spread they meet one another, and form irregularly shaped pearly masses, each of which very early

acquires a yellow centre deeply situated. On cutting into one of the swollen patches at this stage, the pearly tissue is found to be firm and fibrous, whilst the yellow centre is soft and readily broken down. The mass may remain firm and tough, but as a rule the yellow patch becomes larger until it comes almost to the surface; at this period there is a deposit of calcareous salts, which may eventually form a calcareous patch covered by a single layer of endothelium, and by a thin membrane of laminated tissue, which separates the calcareous patch from the blood stream. The swollen or calcareous patches may be separated from the tunica media with the finger nail at almost any time, leaving the media intact.

Examine the contents of one of these small softened centres under a high power (× 300). The fatty or cheesy looking material must be spread out on a slide with a drop of Farrant's solution (§ 98, p. 71), and a cover slip pressed firmly down on it with the handle of a needle. It is seen to consist of (1.) fatty granules and shrivelled fatty-looking cells and fibres; (2.) highly refractile granules, which disappear on the addition of hydrochloric acid (calcareous granuels); (3.) fat crystals; and (4.) crystals of cholesterin, which may be recognised as rhomboidal plates from one corner of which a small square chip is wanting.

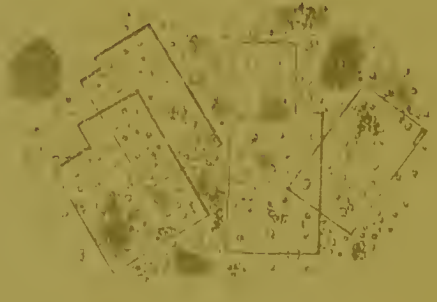


FIG. 42.—Cholesterin crystals, compound granular corpuscles, oil droplets, and granular *débris* (after Cornil and Ranvier).

In more advanced cases the middle coat may be invaded, just as in the case of the cerebral artery already described. Where this is the case, aneurism very frequently results, owing to the weakening of the vessel, the media being the true resistant coat.

Harden a piece of the aorta in Müller's fluid (§ 53, p. 42), or spirit

(§ 52, p. 42), make sections (§ 67, p. 48), stain in picro-carmine (§ 73, p. 53), and mount in Farrant's solution (§ 98, p. 71). It will be noticed, as soon as the section is examined under the low power (× 50), that the intima is on the convex surface of the wall of the vessel, the elastic tissue in the media and adventitia, causing them to contract, so that the outer surface of the vessel becomes concave. This of course would be noticed in time, but it will save time and misunderstanding if it is recognised at once. The next point to be noted is that there is no distinct internal elastic lamina, and consequently no distinct line of demarcation between the intima and the media. In the media, as already stated, there are elastic membranes separating the bundles of muscular fibre one from another.



FIG. 43.—Atheroma of the aorta, stained with picro-carmine. (× 50.)

a. Position of lumen of vessel.
b. Layer in which there is proliferation of cells and swelling of fibres.
c. Commencement of fatty degeneration.
d. Fatty degeneration and calcification in both cells and fibres.
e. Muscular and elastic coat.
f. Do. do. teased out a little, to demonstrate the muscular and elastic layers.

(Note that here there is no internal elastic lamina.)

Commencing immediately under the endothelium, the appearances are very similar to those described in the smaller vessels, except that

the proliferation of cells is not nearly so well marked. Some of the spaces are undoubtedly enlarged, and the once flattened cells have become swollen and are proliferating. The fibres are also swollen. Passing down further, the changes are still very similar, except that the granular and shrivelled looking cells are arranged in more regular layers with the pink fibrous laminæ between,—first a layer of cells, then a layer of fibres, and so on. Deeper still, the fibrous tissue also becomes granular looking; and lastly, just before the muscular tissue is reached, is seen a homogeneous yellow-stained layer with calcareous material (black or bluish grey) deposited in its cracks and spaces. These spaces vary very much in size; some are about two or three times the size of an ordinary cell space only, whilst others are so large that they form a considerable part of the thickening of the intima.

Under the high power (× 300) the flattened cells are seen to be granular looking quite close to the surface, so that they appear to form long, flattened, regular rows of granules. Between these the fibrous tissue is swollen, but it is not markedly granular until some little distance from the surface. After this the changes are almost identical with those examined in the smaller vessel, and the appearances may be interpreted in the same manner. It will be noticed in the majority of sections examined during the earlier stages of the disease that there is a layer of homogeneous pink tissue intervening between the media and the lower and more advanced portions of disintegrating tissue. Here the changes take place in the following order, the most recent being again near the surface, the more advanced, deeper. Near the lumen, there are swelling and proliferation of the cells, which take on the pink stain of picro-carmine deeply; these are followed by swelling of the fibrous laminæ, then by fatty degeneration of the swollen cells, and by a similar change in the fibres. This tissue either breaks down at this stage, or there is a deposit of calcareous material, first in the cells, and then in the fibrous tissue. As these parts in turn become fatty, they lose this power of taking on the pink stain, but take on the yellow picric acid stain. The calcareous particles are more highly refractile, and have a bluish grey colour when examined under the high power. The pink tissue intervening between the broken down calcareous material and the intima is very frequently found to be undergoing fatty degeneration, and small oil

droplets are seen throughout its substance, and although these are not sufficiently numerous to affect the pink colour appreciably, they may be very readily seen scattered at intervals, either in or between the bundles of fibrous tissue. Further, a process of slight fatty degeneration is taking place in the interstitial tissue of the media, in some few cases affecting the internal muscular fibres of that coat.

Endarteritis Obliterans.

149. A more or less acute inflammatory process, which affects especially the intima, also involving the endothelial layer, occurring most frequently as (1.) a syphilitic endarteritis; (2.) the form which is found in healing wounds and in interstitial inflammations, very frequently met with in stone-mason's phthisis; and (3.) a similar form which is found in the vessels of the kidney during the course of Bright's disease (really a form of No. 2).

In syphilitic disease this endarteritis is of extremely common occurrence, and is, according to Heubner and Greenfield, the determining cause of caseating gummata in syphilitic interstitial growths. It occurs especially in the cerebral arteries amongst medium sized vessels, but it may occur in smaller vessels in almost any organ of the body. Along the course of basilar artery, for instance, in which there is such a condition, small nodular thickenings make their appearance; these thickenings are frequently asymmetrical, so that the lumen of the tube affected may be very irregular in shape and very much contracted. In some cases clots are found in the lumen, but these are frequently *post mortem*. Harden in spirit (§ 52, p. 42).

On examining a section stained in picro-carmine (§ 73, p. 53), and mounted in Farrant's solution (§ 98, p. 71), under a low power (× 50), the principal site of the thickening is seen to be in the intima, internal to the elastic lamina. At the same time there appears to be some slight infiltration of the adventitia with cellular elements. The middle coat is generally irregularly thinned.

The thickened intima is made up of numerous cells, which appear to be formed by proliferation of the endothelial cells, and of the flattened cells of the intima. As already stated, this proliferation may become so great that the lumen of the vessel is almost obliterated.

Examine under a high power (× 300). Lining the vessel is a layer of more or less flattened cells, which have a spindle shape when seen in section, or some of them may be rounded. Beneath this is a layer of irregular cells, some with rounded and others with elongated nuclei, whilst deeper still, and next to the internal elastic lamina, is a layer of flattened cells, with here and there a group of rounded cells. Pushing their way into this mass of cells are numerous capillary blood-vessels, which are passing through the internal elastic lamina, from the capillaries of the inner layers of the media. It will be at once noticed that the condition is one of organisation of a granulation tissue; and where the process has lasted for any considerable length of time, imperfectly developed fibrous tissue is formed (see Fig. 45, near *a*., where there are fibrous laminæ, between which are spaces,

FIG. 44.—Section of the inner coat of a small syphilitic artery. (× 170, after Greenfield.)

a. Lumen of the vessel.
b. Internal elastic lamina.
c. Thickened and cellular inner coat.
d. Situation of muscular coat.
e. Layers of cells representing endothelium.
f. Transverse section of a small vessel in the deeper part of the inner coat.

some containing cells, others empty). No fatty degeneration is found in this form. Organisation in clot in a vessel will be described under the head of healing of wounds.

In almost all cases of endarteritis obliterans syphilitica, as in the similar condition in interstitial nephritis, there is a considerable amount of thickening of the adventitia, and even of the surrounding

connective tissue, accompanying the changes in the intima. This is seen either as a small round-celled growth, or the mass of round cells



FIG. 45.—Drawing of small segment of section of a syphilitic artery. (× 170, after Greenfield.)

a. Lumen of the vessel.

b. Internal elastic lamina.

Between *a* and *b* the enormously thickened intima, *c*, divided into two areas by a secondary elastic lamina, *g*.

d. Muscular coat thinned near *b*, considerably encroached upon by the small round-celled growth in the intima.

e. Adventitia, cellular and thickened, in which are numerous blood-vessels, *h*, prolonged through the media, and into the deeper layer of the intima, *i*.

has become organised into more or less completely developed fibro-connective tissue, and may be recognised as such under the microscope.

Changes which take place in the Middle Coat of the Vessels.

150. Of these several have been already mentioned as occurring in connection with disease of the intima, and the only one to be mentioned here is calcification of the middle coat, which occurs especially in the medium sized vessels of elderly people, and is found in these vessels where at the same time there is a condition of endarteritis deformans in the aorta. In an early stage this change consists of a fatty degeneration of the muscular wall of the artery, which makes its appearance as yellow patches or circles in the deeper part of the wall; this gradually spreads, but before the patches run together a deposit of calcareous material takes place in the fatty yellow rings. Later, the whole muscular wall becomes first fatty and then calcareous. The muscular coat is represented simply by a brittle tube. If this be macerated a perfect cast of the muscular coat remains.

Make sections of such a vessel after hardening in Müller's fluid (§ 53, p. 42), and stain one in picro-carmine (§ 73, p. 53); another section may be stained with osmic acid (§ 80, p. 62). Mount both in Farrant's solution (§ 98, p. 71).

Under a low power (× 50) the muscular coat is seen to be undergoing fatty degeneration, the tissue appearing yellower (with picro-carmine), or blackened (with osmic acid.) The intima and adventitia are almost normal in appearance.

High power (× 300).—The media is in a state of fatty degeneration at certain points, the muscular fibres are granular and much yellower than normal, whilst with osmic acid a number of these granules are stained black.

At other parts refractile granules are seen. These, when treated with hydrochloric acid, disappear with the evolution of carbon dioxide. Here again the intima and adventitia are comparatively healthy, though the adventitia in some cases appears to become infiltrated with cells, and is weakened, this occurring secondarily to rupture of the brittle tube.

A similar condition of calcification is frequently met with in the smaller arteries, as at the base of the brain, where, however, the calcareous patches have a peculiar annular arrangement. The micro-

scopic appearances of a transverse section are exactly the same as above. The fatty degeneration of the vessels which takes place in phosphorus poisoning has been already referred to (see § 114, p. 88.) This takes place especially in the capillary vessels, where first the protoplasm around the nucleus becomes granular, and then droplets of fat are formed in the cells which form the wall of the vessel. These are stained black with osmic acid, and may come to occupy the whole of the cell. Punctiform hæmorrhages are found where the vessels give way under increased pressure. The fatty degeneration may extend to the smaller arterioles, and, like the following condition, greatly predispose to the formation of aneurisms and ruptures of vessels. Waxy degeneration in this position is met with, especially in the small arterioles. See descriptions of waxy organs.

Chronic Periarteritis, or Inflammation of the Adventitia.

151. This occurs along with endarteritis, as already mentioned, in interstitial inflammation (Kidney, Lung, &c.), and will be mentioned with the changes which take place in those organs. It is specially met with in syphilitic interstitial inflammations, and forms a marked feature in such cases; but the most important form of the disease is that which occurs in the adventitia of the small arteries of the brain. It consists of a chronic inflammation of the adventitia, most frequently associated with endarteritis and a gradual atrophy and degeneration of the middle coat, all of which changes may be readily observed under both powers. The outer coat is formed of laminæ of fibrous tissue, between which the connective tissue cells may be seen as flattened corpuscles, whilst the middle coat becomes granular looking, is very much compressed, and condensed. Where this condition is present, multiple aneurisms and hæmorrhages are of very frequent occurrence.

152. Whilst the subject of vessels is under consideration, it will perhaps be well to give very briefly the various forms of aneurism which are met with as a result of injury or disease to the walls of the vessels.

True Aneurisms.

A true aneurism occurs where the vessel is dilated so as to form a sac, the walls of which are formed by some or all of the coats of the vessel, generally by parts of the intima and the adventitia. The blood is thus confined within its proper walls, but not within its proper bounds. Anything which weakens the wall of the vessel may give rise to this condition.

Cylindrical and fusiform aneurisms are formed as longer or shorter symmetrical dilatations of the vessel. They occur in atheroma and arteritis, affecting the whole wall of the vessel for a longer or shorter distance. This condition is accompanied by thinning of the media, flattening of the intima, and distention of the adventitia, the last-named of which forms the chief part of the wall of the aneurismal sac.

Sacculated aneurism is the form in which there is an unilateral dilatation of the wall of the vessel, the opening being generally smaller than the cavity into which it opens. Where this cavity is formed, the muscular coat has disappeared, the intima appears as a modified flattened coat, and the adventitia is composed of thickened fibrous laminæ, between which are found flattened cells. The thickened adventitia forms the principal part of the wall of the aneurism. (It is generally lined by or filled with a laminated clot, and frequently occurs as a result of localised endarteritis.)

Dissecting aneurism commences suddenly, and is due to rupture of the brittle intima. The blood makes its way between the layers of the media. It may pass for some distance down the vessel, and then make its way into the lumen again. This form may be developed as one of the results of the fusiform dilatation, or it may be found where there has been chronic inflammation of the wall of the vessel, especially of the intima.

Saddle-clot aneurism.—A sacculated aneurism, which is found at the bifurcation of a vessel. It is frequently due to the endarteritis set up by an embolus arrested at the point of bifurcation of the vessel.

Miliary aneurisms.—Multiple sacculated aneurisms, occurring in the brain as a result of fatty degeneration or of periarteritis, in either of which conditions the coats of the vessels are weakened at many points.

False Aneurism.

A false aneurism is a cavity formed in connection with the lumen of a vessel. This cavity, however, is not bounded entirely by the coats of the vessel, but communicates with some other cavity, or its walls are formed by external tissues.

Traumatic aneurism is formed where a vessel is wounded and the blood escapes into the surrounding tissues, gradually displacing them until they form a limiting wall around the vessel. There may be pulsation in a cavity so formed. A true aneurism may by rupturing form a false aneurism; as the blood may escape into and distend the tissues until a second cavity is formed outside the first.

Varicose aneurism is a form where a true aneurism opens into a vein, or where a false aneurism communicates with a vein. When venesection was more frequently practised this form was especially common at the bend of the elbow.

Aneurismal varix is the condition in which a false aneurism is formed in the vein. There is a direct communication between the vein and the artery, and whilst the latter remains comparatively undilated, the vein becomes enormously distended, in consequence of the direct throwing in of the arterial blood.

Other conditions which simulate aneurism, but which do not come under either of the above headings, are—

(1.) The *cirsoid aneurism*, which consists of a number of small arteries, veins, and capillaries, which are elongated, dilated, and frequently varicose. The whole mass of vessels forms a pulsating tumour.

(2.) *Aneurism by anastomosis*, where, along with enlargement of existing arteries, new arteries are formed, and a pulsating tumour is the result.

The wall of an aneurism is found to be composed almost entirely of laminated fibrous tissue. Between the laminæ are flattened cells. Some of this tissue is the persisting intima, other parts, the more important, the altered adventitia. Patches of granular and fatty media may be seen near the undilated vessel, or where the dilatation is but slight, but in most parts it has disappeared almost entirely. In some cases the wall of the aneurism is calcified.

Diseases of Veins

Are very similar to those of the arteries.

Varix.

153. This is a condition in which the superficial veins, especially of the lower extremities and of the mucous membranes, are seen to become distended and tortuous. Irregular dilatations, or ampullæ, occur along their course, whilst here and there calcification of the wall takes place. On slitting open such a vein, the valves are found to be obliterated by the stretching of the intima, the valvular folds being drawn out. Surrounding the tortuous and dilated veins is usually a more or less dense mass of connective tissue, which mats the vessels together. Harden one of the larger veins in Müller's fluid (§ 53, p. 42); make sections (§ 67, p. 48). Stain a section with picro-carmine (§ 73, p. 53), and mount in Farrant's solution (§ 98, p. 71).

With the low power (× 50) the inner coat is seen to be composed of laminated tissue, almost identical in structure with that described in endarteritis deformans. The longitudinal and transverse bands of muscular fibre, stained yellow, are surrounded by pink connective tissue, often containing golden-brown altered blood pigment. The adventitia is also somewhat thickened. Where the dilatation is very great and irregular, the muscular bands may have entirely disappeared at the points of dilatation, or they can only be seen as granular or fatty masses scattered throughout the laminated connective tissue.

These appearances must be verified under the high power (× 300).

Organisation in clot in veins takes place in the same manner as in arteries, and will be referred to in the description of healing of wounds.

CHAPTER VI.

THE KIDNEY.

154. This organ in its normal condition is "smooth, and of a deep red colour." It is about four inches long, two and a half inches broad, and one and a quarter inches thick, though the left kidney is somewhat longer and narrower than the right, and is also rather heavier. On close examination of the surface of the organ, small injected stellate veins are seen beneath the capsule. To strip off the capsule, the better plan is to commence by making a longitudinal incision from the convex border to the hilus, then to lay hold of the capsule with the fore-finger and thumb and strip it off. In the normal condition this is readily done; the surface then has a homogeneous appearance, streaked with the stellate veins. On examination of the section made as above, the kidney is seen to consist of (1) the cortex, forming the outer layer of tissue; and (2) the medulla, or the part between the cortex and the pelvis of the organ. The relative proportion of these parts is as three and a half to six and a half, or, more roughly speaking, one to two. Radiating from the medulla to the surface in the cortex are numerous sets of parallel straight lines. These, on close examination, are found to be small arterial trunks, on each side of which are arranged, very regularly, a number of small round shining masses—the Malpighian bodies. Between them are opaque conical bundles of straight tubes. The straight tubes are longest midway between the rows of Malpighian bodies, and reach nearly to the surface, but nearer the Malpighian bodies they are considerably shorter. This structure will be examined more in detail under the low power of the microscope. On each side of the straight tubes is a somewhat irregular mass, composed of sections of convoluted tubules. At the line where the cortical substance joins the medulla are numerous sections of vessels of considerable size, from which, as will be seen later, branches pass both upwards and downwards.

The medullary portion of the kidney may, for the sake of convenience, be divided into two layers, the boundary layer and the papillary portion. "Each papilla, with the section of boundary layer belonging to it, forms a pyramid of Malpighii" (Klein). These pyramids of Malpighii, of which about eight are usually seen in the section, extend as inverted cones from the papillary part to the superficial cortex, and between the bases of these pyramids the cortex dips down for some distance, as far as the bases of the papillæ forming the so-called interpyramidal cortex. The pyramids are made up of a series of alternating light and dark lines, the light lines being the urinary tubes, and the dark lines the straight vessels, proceeding from the boundary area to the apices of the papillæ. The light lines are continuous with the conical bundles of tubules, which have been described in the cortex.

The papillary portion of the pyramid is considerably lighter in colour than the cortex, which is described as being "light crimson brown." It consists of a markedly striated tissue, the striæ regular, and at right angles to the openings of the papillæ, as they open into the calyces.

Much is to be learned from a naked eye examination of the kidney. Such examination should be most systematically carried out. Attention has already been drawn to the general appearance, and the more minute details will be considered in treating of the separate diseases. For the purposes of the pathologist, the kidney may be described as consisting of a series of lobules, and any change which is found in one of these lobules may confidently be looked for in any other. But, before describing the lobule, it will be necessary to have some idea of the various structures of which it is composed.

Blood-vessels.—The arteries run from the pelvis along the sides of the Malpighian pyramids in the submucous tissue, and enter the substance of the kidney at the boundary layer, at once breaking up into a number of arches, the convex surfaces of which are upwards; from these arches two sets of vessels pass, one upwards, the interlobular arteries, and one downwards, branches which subdivide to form the arteriolæ rectæ. The interlobular arteries give off a series of lateral branches (afferent arterioles) almost at right angles, and each of these passes to a Malpighian body, where it breaks up into a glomerular tuft, or a tuft of small capillary vessels. These are again

collected into a single vessel, which carries the blood from the

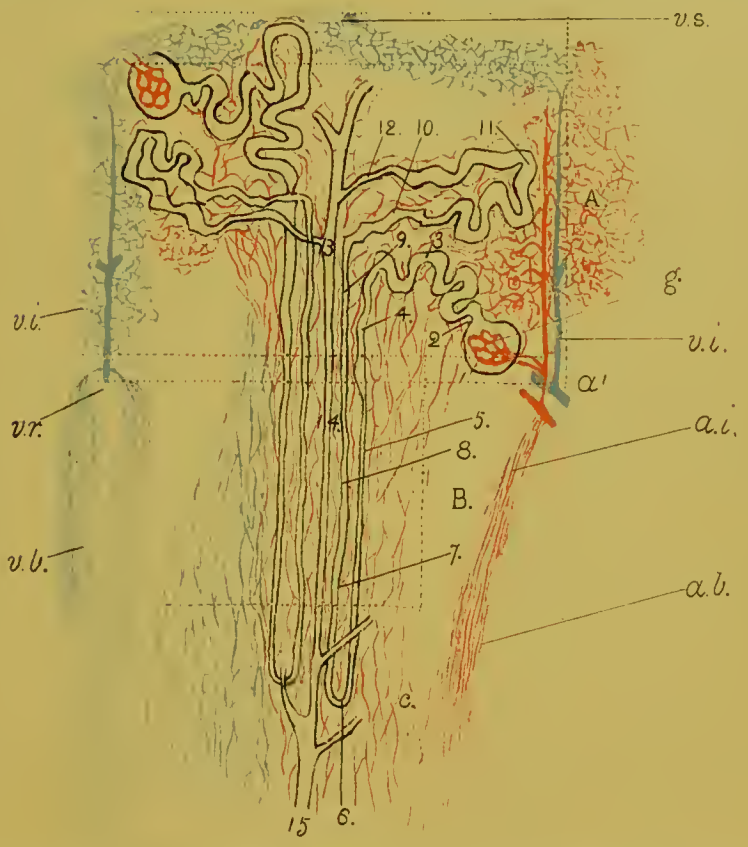


FIG. 46.—Diagram showing the course of the renal tubules, the arrangement of the vessels, and the Malpighian bodies. (Modified from Klein and Noble Smith.)

v.s. Stellate vein.
v.i. Interlobular vein.
a.i. Interlobular artery.
g. Glomerulus of Malpighian corpuscle.
a.r. Arteria recta.
v.r. Vena recta.
a.b. Bundle of arteriolæ rectæ.
v.b. Bundle of venæ rectæ.
A. Cortex.
a. Subcapsular layer, not containing Malpighian corpuscles.
*a*¹. Inner layer of cortex, not containing Malpighian corpuscles.
B. Boundary layer.
C. Papillary part.

1. Bowman's capsule.
2. Neck.
3. Proximal convoluted tubule.
4. Spiral tubule.
5. Descending limb of looped tubule of Henle.
6. The loop.
7. Ascending limb.
8. Spiral part of ascending limb.
9. Narrow part in medullary ray.
10. The irregular tubule.
11. Distal convoluted tubule.
12. Curved collecting tubule.
13, 14, 15. Straight collecting tubule.

Malpighian corpuscle (the afferent arteriole) and then breaks up to form a network of capillaries ; these capillaries surround the tubules of

various forms, and afterwards open into veins, which gradually unite to form the interlobular vein. In addition to the above branches of the artery and vein, there are interstitial and capsular branches, and the interlobular vein commences as the stellate vein already described. It is necessary to remember this fact in connection with chronic venous congestion of the kidney.

Passing downwards into the medulla from the arches in the boundary layer are numerous short vessels, which speedily break up, each one into a tuft or pencil of small straight vessels, the arteriolæ rectæ; these form a network, with elongated meshes around the bundles of urinary tubules; they pass down as far as the papillæ. Commencing at the apices of the papillæ are small veins which return to the boundary layer, and take a similar course to the arteriolæ rectæ, but on the opposite side of the bundle of straight tubules. In the boundary layer, the blood from these meets the blood from the interlobular veins, and is conveyed away from the kidney by large venous trunks in the submucous tissue to the hilus, and thence by the renal vein.

Urinary tubules.—Forming the parenchyma, or substance proper of the kidney, are the urinary tubules. Klein describes these as commencing "with a coacal extremity in the Malpighian corpuscles," and terminating "with an opening on the free surface of the papilla." He then goes on to describe the tubules as composed of sixteen different segments, the first of which, (1) the Malpighian corpuscle, is in reality the invaginated and distended end of the blind tube (like the finger tip of a glove turned inwards). Pushed into the invagination is a tuft of capillary vessels communicating on the one hand with the afferent arteriole, and on the other with the efferent arteriole, both of which pass into the involuted "tip." The outer coat of the double covering of the capillary tuft is known as Bowman's capsule. It is composed of a basement membrane, covered on its external surface with a quantity of connective tissue, whilst internally it has a layer of flattened endothelioid cells. Continuous with this layer of Bowman's capsule is a similar layer of flattened cells covering the tuft of capillaries, forming what is in fact a reflection of the capsule. Supporting the capillary vessels is a delicate connective tissue framework, the nuclei of the cells of which are

readily distinguished in stained specimens. Between the tuft of capillaries and Bowman's capsule is a space which communicates by (2) a narrow opening, or neck with the tubule proper. The



FIG. 47.—Malpighian body, and part of convoluted tubule of kidney of dog. (× 350.) (After Klein and Noble Smith.)

a. Capillaries of the glomerular tuft arranged in lobules.
b. "Bowman's capsule, with its lining of flat epithelial cells, and the flat epithelial cells covering the glomerulus."
s. Stalk of the glomerulus, composed of afferent and efferent arterioles.
n. "Neck of the Malpighian corpuscle."
c. Longitudinal section of first part of the convoluted tubule.

tubule throughout its whole extent is composed of a basement membrane, and resting on this is a layer of epithelial cells, which vary very considerably in form and structure in the different sections of the tube. In the neck of the tubule the cells are slightly cubical in form, but those nearest the glomerulus are flattened. Immediately following the neck, and therefore near the Malpighian body, comes (3) the first convoluted tubule, which, with the following part, (4) the spiral tubule, runs entirely in the cortex. In these the epithelium is columnar, and each cell has a rounded nucleus situated at about the centre of its substance. Here the epithelium is not quite regular, especially in the spiral tube, where some of the cells are narrow, "with concave sides," while others are broad and projecting, "with convex sides and convex free surfaces." The next part of the tubule (the looped tubule of Henle) is principally within the

medulla. The descending limb and the loop itself, (5) and (6), are lined by a layer of flattened epithelial cells. After the loop the ascending limb of the tube (7) is lined by a layer of columnar cells,



FIG. 48.—Looped tubes of Henle cut longitudinally in both the boundary layer and the papillary portion of the pyramid. (× 300.) (After Klein and Noble Smith.)

a. First part of the ascending limb of the looped tube of Henle, in which the epithelium is cubical.
b. Part of the ascending limb.
c. The bend.
d. The descending limb of the looped tube of Henle, in all of which the epithelium is flattened and squamous looking. The tubules at these points are very like young blood-vessels in appearance.

each of which has its nucleus placed near the lumen. Passing further upwards (8) the lumen becomes narrowed, but the epithelium remains columnar. In the cortex (9) the ascending tube is narrower, and its epithelium more cubical or flattened. Still in the cortex is (10) the irregular tubule, lined by columnar cells, which vary very much in height, but always leave the lumen of this part of the tube very

narrow. It opens into (11) the second or distal convoluted tubule, which is "identical" in position and structure with the first part of the convoluted tubule. After this, still in the cortex, are (12) the curved parts of the collecting tubule, and (13) part of the straight tubule, the lining of which is an irregular epithelium, with some of the cells cubical, others spindle-shaped, but all having well-marked nuclei. Lower down in the medulla (14) the lumen of the tube is larger and the cells are cubical or slightly columnar, and each contains a spherical nucleus. (15) The lower parts of the collecting tubes, and (16) the large papillary ducts, are lined by epithelium of a cubical type, leaving the channels in these tubules of considerable size.

From the accompanying diagram and description it will be seen that, the straight collecting tube being taken as a central point, the looped tubules of Henle are arranged on each side of it, whilst further out come the sections of the two convoluted tubules, and lastly the Malpighian bodies as they spring from the interlobular arteries. A lobule of the kidney is composed of the whole of the tissues between two interlobular arteries and the prolongations of these down into the medulla.

The lobule of the kidney may, like the lobule of the liver, be divided into three zones. In the peripheral zone are the Malpighian bodies, with irregular sections of the convoluted tubules, in which the epithelium is columnar, and the opening small. The intermediate zone, which is much smaller, is made up of convoluted tubules alone, lined with cubical epithelium, the opening of the tubule still remaining narrow. In the centre of the lobule the straight tubule and the larger collecting tubes are seen, in which also the epithelium is cubical, but the lumen is comparatively large.

In the medulla these lobules are continued downwards, but of course without the peripheral and intermediate zones, as the Malpighian bodies and most of the convoluted tubules are found in the cortex only. The central zone is continued into the medulla, and is composed, as in the cortex, of the straight tubules, with cubical epithelium and comparatively wide lumina, of the descending limbs of the looped tubule, with wide lumina and the epithelium flattened, and of the straight collecting tubules. In the greater part of the papillary portion of the medulla the lobule is represented by these collecting tubes alone.

Examine a section of the cortex of an injected kidney (§ 40, p. 34), taken in the plane of the convex outer surface.

Low power (× 50).—A number of polygonal areas are observed, bounded by vessels, with Malpighian bodies here and there, in which the capillaries are injected. Within this vascular ring are numerous sections of tubules, some of them cut obliquely, others more transversely. Note that the lumen of each tubule is small and irregular; the epithelium is slightly columnar, with a rounded nucleus near the lumen; the vascular meshes around these tubes are of considerable size. Nearer the centre are the tubes described as in the intermediate zone, and here the loops of vessels are smaller, as the tubules are not only smaller, but are cut transversely more regularly. In the central zone the meshes of the network of vessels are again somewhat larger.

With the same power (× 50) examine a section cut at right angles to the above (this is the direction in which sections of the kidney are usually made). The zones of the lobules, as above described, can be made out in both the cortex and medulla. Notice especially the large vascular meshes around the convoluted tubules in the peripheral and intermediate zones, the more elongated meshes around the tubules (seen now in longitudinal section) of the central zone; in the medulla, the long vascular bundles and meshes running down, between, and around the bundles of straight tubules. Examine further under the high power the arrangement of the tubules with their contained epithelium, the structure of the Malpighian bodies, the amount of connective tissue within the capillary loops of the glomerulus, and any other features described above.

Chronic Venous Congestion of the Kidney.

155. *Synonyms.*—"Cyanotic" Kidney (not a good term), "Congestive Induration," "Passive Hyperæmia" of the Kidney.

This form of kidney is met with in valvular disease of the heart, more especially with mitral disease, in chronic fibroid phthisis, chronic bronchitis, emphysema, &c., in fact under just the same conditions as chronic venous congestion of the liver (§ 116, p. 94), to which this is analogous.

In cases of heart disease, during the course of which albumen in the urine or slight hæmaturia has been present, this condition may very frequently be found after death. In the earlier stages of the congestion the kidney is enlarged, and may be as much as seven or eight ounces in weight.

Under the capsule, the venæ stellatæ are considerably distended and very prominent; the whole organ is firm and elastic or tough feeling. On making a section into it at a plane at right angles to the convexity of the kidney, the capsule is very readily removed; the cortex is smooth, considerably congested, and at first a deep purple colour, which rapidly turns to crimson.

On examining the cortex more carefully, it is found to be slightly increased in size, the Malpighian bodies are very prominent as red spots, regularly arranged in parallel rows on each side of the prominent interlobular vessels (distended interlobular veins). The most marked changes, however, are in the medulla, where the venulæ rectæ stand out prominently, especially at the bases of the pyramids, which are deeply congested, and the tissue has a very distinctly striated appearance, the congested vessels shining out very prominently between the bundles of uriniferous tubules. In old-standing congestion irregular pale patches may make their appearance, and the organ may feel almost fibroid.

Harden a piece of such a kidney in Müller's fluid (§ 53, p. 42); cut (§ 67, p. 48); stain a section in picro-carmine (§ 73, p. 53), and mount in Farrant's solution (§ 98, p. 71). The following description applies to the later stages of the disease (in the earlier stages there is simply the distention of the vessels without any of the structural changes).

Examining a section under a low power (× 50), it is seen that the interlobular veins in the cortex are filled with a greenish looking material, which will be afterwards recognised as composed of coloured blood corpuscles. Following the course of these veins, it is seen that the capillary plexus between the convoluted and straight tubules is also distended with blood, and that the efferent arterioles and the glomerular capillaries are similarly affected. The glomeruli are, in some cases, very much increased in size, whilst the connective tissue nuclei are increased in number. In the medulla the straight vessels are extremely prominent, and are all filled with this coloured blood.

Next examine the tubules. Very frequently the capillaries in the Malpighian bodies show signs of rupture, small extravasations of blood are to be seen in the capsule, and large masses of altered blood may be seen in the convoluted tubules. In the straight tubules in the medulla small masses of golden brown pigment are met with, and here and there almost inky black "melanin" casts are seen occupying a few of the tubules in the papillary portion of the medulla. The epithelium in some cases nearly fills the tubule, but at some points it is granular looking, with small globules of fat in the protoplasm of the cell. This is by no means a constant condition. Very

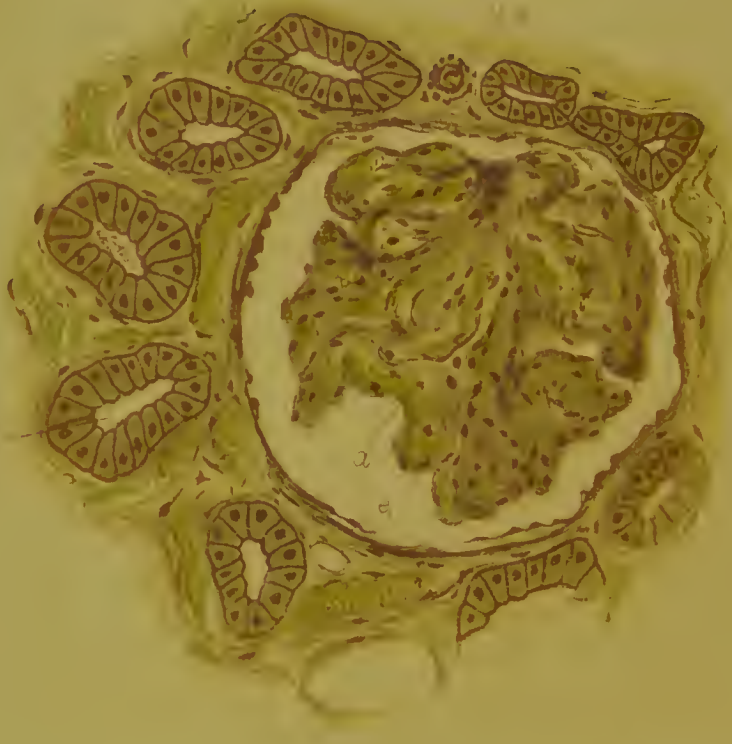


FIG. 49.—Drawing of section of cortex of kidney in a state of chronic venous congestion. Stained with logwood. (× 300.)

a. Capillaries of glomerular tuft distended with blood.
b. Intertubular capillaries in a similar condition.
a.a. Afferent arteriole seen in transverse section.
c.t. Convoluted tubules.
c. Flattened cells lining Bowman's capsule.

It will be noticed that there appears to be a considerable thickening of the walls of the vessels between the sections of the convoluted tubules.

frequently wedge-shaped pink patches of fibro-cellular tissue are seen under the capsule, extending at their apices for some little distance

into the substance of the kidney. They extend along the lines of the interlobular vessels, and may enclose the Malpighian bodies, which then become atrophied and fibrous in appearance. In the same manner the tubules involved in these masses are atrophied and small, and their epithelium flattened. This is said to be an intercurrent condition, but it is one which frequently occurs in this disease.

Examine under a high power (× 300). The capillary tufts in the Malpighian bodies are greatly enlarged and the vessels distended. The coloured corpuscles are now readily distinguished as green rings occupying the dilated capillaries. In a few of the Malpighian bodies, between the tuft and Bowman's capsule, blood corpuscles in various stages of breaking down may be seen. Frequently there appears to be a slight increase, not only in the number of connective tissue nuclei, but also of the pink fibrillated tissue around the walls of the capillaries.



FIG. 50.—Drawing of section of kidney (boundary layer) in a state of chronic venous congestion. Stained with picro-carmine. (× 300.)

v.c. Vessels distended with coloured blood corpuscles.
a.l.H. Ascending limb of looped tubule of Henle. Spiral portion and collecting tubule.
d.l.H. Descending limb.

The investigator next comes to the convoluted tubules. The epithelium is comparatively healthy, though in some cases it is under-

going cloudy swelling, or even fatty degeneration. In the lumen of a tubule small collections of broken-down blood corpuscles, or golden brown pigment, are frequently seen. These are derived from the small hæmorrhages which have been already described in the Malpighian bodies. The vessels are greatly distended between the tubules with blood corpuscles, seen as the green globules. The walls of these vessels are also thickened, and take on a pink reaction with the carmine, just as in the case of the thickened vessels in "Nutmeg Liver." In the medulla the longitudinal and transverse sections of the straight vessels are filled with blood, the walls are thickened, and are stained pink. In the tubules the epithelium is frequently undergoing some degenerative change, though this is by no means an invariable condition. There may be fatty globules in the cells, or these cells may be undergoing proliferative changes. Here, too, are found the "melanin" casts already referred to as composed of the altered blood pigment.

The wedge-shaped patches are seen to be composed of pink fibrous tissue, with a few round cells at the margin. The Malpighian bodies in them are atrophied and fibrous looking (see Interstitial Nephritis), whilst the enclosed tubules are small, and the epithelium lining them is flattened, extremely granular, and atrophied. In some of the cells small globules of fat are seen, which may be stained with osmic acid. The study of these sections will give an exceedingly good idea of the vascular supply of the kidney.

The above mostly mechanical changes commence in the veins, the interlobular and the straight veins being first affected, afterwards the capillaries and then the arteries. Distention and thickening of these take place as in "Nutmeg" liver. The changes in the epithelium ensue in the later stages, and are due, in great measure, to malnutrition.

Fat Embolism of the Kidney.

156. This occurs in some cases of diabetic coma, or in a similar coma brought on by fracture of bones, especially of the bones of the head. In both these conditions there is fat circulating in the blood, which is eventually arrested in some of the smaller vessels.

The naked eye appearances vary considerably, but the points which must be looked for are pallor, increased size, and flabbiness of the organ, and minute hæmorrhages under the capsule or on the surface of the sections.

Where this condition is suspected make a microscopic examination at once. To make a more exhaustive examination put a piece of the organ to harden in Müller's fluid (§ 53, p. 42), cut (§ 67, p. 48); stain a section with osmic acid (§ 80, p. 62), and then with picro-carmine (§ 73, p. 53); mount in Farrant's solution (§ 98, p. 71), and examine under the low power (× 50). There is evidently some congestion, especially at certain points. Near these congested areas are black masses, filling some of the vessels between the tubules, evidently fat stained by osmic acid. Similar black masses are also seen in some of the capillaries in the glomerular tuft, and in the straight vessels. Near the congested areas, too, are small hæmorrhages; from these some of the fatty material may have escaped into the surrounding tissues, or into the tubules, especially where the rupture has occurred in the Malpighian tuft.

These appearances are to be verified under the high power (× 300), special care being taken to localise the fat in the vessels above mentioned. The hæmorrhages are also to be carefully examined under this power.

Waxy Kidney.

157. This disease may be, and frequently is, associated with other marked changes of the tubules and of the interstitial tissue, but as these are rather superadded diseases, it will be well to confine the description to the pure waxy change, and take up the other conditions separately. For example, waxy disease is frequently associated with interstitial nephritis, in which case the changes due to the waxy condition are to a certain extent masked by those due to the interstitial disease. For conditions under which this disease occurs, see Waxy Liver (§ 115, p. 94).

Naked eye appearances in the early stage of this disease.—The organ is usually slightly enlarged, and the capsule strips off very readily; the surface is smooth, glistening, anæmic, and often yellow. On cutting into the kidney the cortex is pale and anæmic, and in it are seen the

Malpighian corpuscles as glistening rounded bodies, arranged regularly in parallel rows, whilst the surrounding tubular tissue has a peculiar mottled look, though there are no very marked evidences of fatty degeneration.

In the medulla the appearances are also very characteristic. The striation is slightly exaggerated at the base of the pyramid, and there is usually, even in this early stage, a comparatively deep colour, due to congestion in this position, the apices of the papillæ remaining pale.

Pour a watery solution of iodine (§ 77, p. 61) over the fresh surface of the section, and note that dark mahogany lines make their appearance in the position of the straight vessels, and that the glassy looking Malpighian bodies also take on this brown staining. In an earlier stage, where otherwise no naked eye changes are distinguishable, the iodine staining frequently brings out the fact that there is slight waxy degeneration in the Malpighian bodies and in the walls of the straight vessels.

Harden a piece of kidney in the above stage of waxy degeneration in methylated spirit (§ 52, p. 42), cut sections (§ 67, p. 48), and mount one unstained. Stain others with iodine (§ 77, p. 61) or methylaniline violet (§ 76, p. 59), mount this latter in Farrant's solution (§ 98, p. 71) or in acidulated glycerine (§ 93, p. 68).

Examine the unstained specimen under a low power (× 50). The Malpighian bodies are enlarged, and have a translucent appearance. This translucent appearance does not extend throughout the whole of the capillary tuft, but certain of the capillary vessels only are affected. Their walls are thickened, homogeneous, and glassy looking, and have a yellow tinge; the transverse diameter of the vessel as a whole becomes increased. Parts of the tuft remain perfectly healthy, so that there is a kind of picking out of the tuft with the waxy material. Examine the afferent arteriole, and note that it also is affected, small areas of the middle coat becoming quite glassy looking, and in the medulla the arteriolæ rectæ are undergoing similar changes.

In the methylaniline violet stained section the waxy parts are stained red violet, and the normal tissues blue. In this stage of the disease the changes in the epithelium lining the tubule are comparatively slight, but in the advanced stage, under which they will be

considered, such changes are far more marked. As a result of epithelial changes, however, colloid casts may be found even in this early stage. These casts are perfectly homogeneous in appearance; they fill up the lumen of the tubule, and the epithelium around them is usually considerably flattened. Find such a cast, unstained or stained with iodine, and it appears to be very like the waxy material, but, stained with methylaniline violet, it gives a blue violet reaction instead of a red violet, as it would if it were of a waxy or lardaceous nature.

Examine the same sections under a high power (× 300), note the

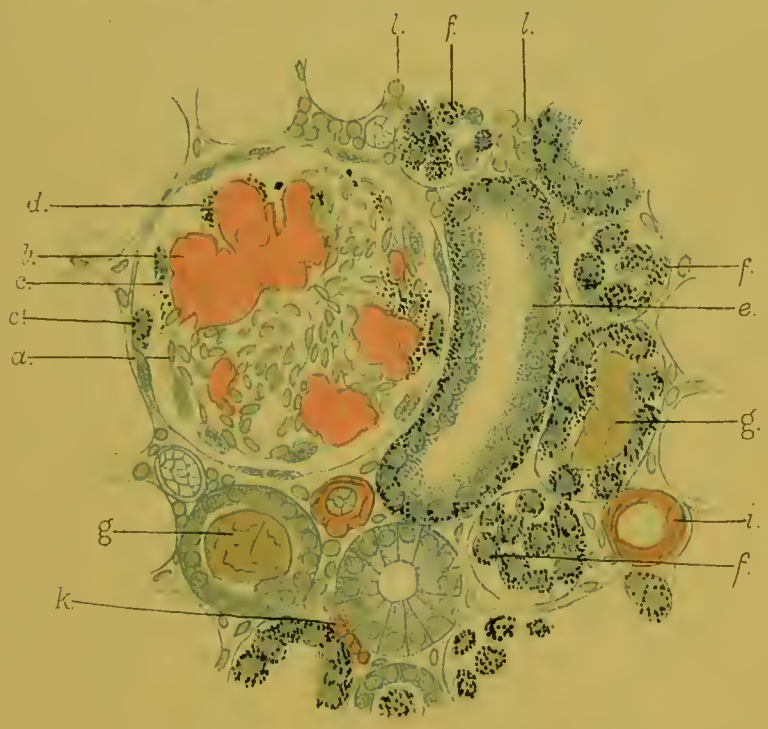


FIG. 51.—Waxy and fatty degeneration of the kidney (after Ziegler). (× 300.)

a. Normal capillary loop.
b. Waxy capillary loop.
c. Fatty epithelium of the glomerulus.
*c*¹. Fatty epithelium of the capsule.
d. Oil drops on the capillary walls.
e. Fatty epithelial cells *in situ*.
f. Loosened fatty epithelial cells.
g. Colloid masses (forming casts).
h. Fatty cast in section.
i. Waxy artery.
k. Waxy capillary.
l. Infiltration of connective tissue with leucocytes.

patches of waxy material in the walls of the capillaries in the glomeruli, and see that here the flattened cells and the basement

membrane of Bowman's capsule are unaffected. In the muscular coat of the afferent arteriole observe the swollen and translucent (or red violet) patches. Note that although the diameter of the whole vessel is increased, the lumen of the vessel is diminished in size. Note, too, the marked changes in the arteriolæ rectæ, and that the vessels near the papillæ are more affected than those near the base of the pyramid. If this be remembered when the naked eye examination is referred to, the fact that the base of the pyramid is relatively deep in colour will be understood. This diminution in the diameter of the vessels also suggests the cause of the pallor of the organ, even in the early stage. Further, not only is the quantity of blood passing through the organ lessened, but from the nature of the causes of the disease, the quality of the blood is very much deteriorated. To these two conditions the fatty changes which occur during the later stages of the disease are also to be referred. The appearances of the colloid casts as above described must be verified under the high power, and the chemical and colour reactions again observed. The epithelium is comparatively healthy throughout, though even at this stage slight fatty degeneration has in a few cases supervened.

Waxy Kidney—More advanced Stage.

158. In the later stages the kidney is very soft and flabby feeling; it may be enormously enlarged, attaining even twice its usual size. The capsule strips off readily, the surface is smooth and pale, having a dull brown or brownish yellow colour as a groundwork, over which there are numerous pale patches, giving it a pale mottled appearance. On section, the great increase in size is seen to be due, in great measure, to the increase in the size of the cortex. The Malpighian bodies are enormously swollen, and stand out prominently as large glistening masses. With a hand-lens the vessels between the tubules are also seen to be glistening and swollen, whilst the tubules themselves are pale and fatty looking. The striation of the medullary rays is very well marked, and the basal congestion is fairly well seen. The tips of the papillæ are especially pale. Pour a watery solution

of iodine over such a surface. The mahogany brown staining is very diffuse. The Malpighian bodies, the interlobular arteries, the intertubular plexus, and the straight vessels in the medulla are all affected. Harden a piece of this kidney in methylated spirit (§ 52, p. 42), make sections (§ 67, p. 48), and examine one unstained, a second stained in iodine, and mounted in iodine mounting fluid (§ 77, p. 61), and a third stained in methylaniline violet (§ 76, p. 59), and mounted

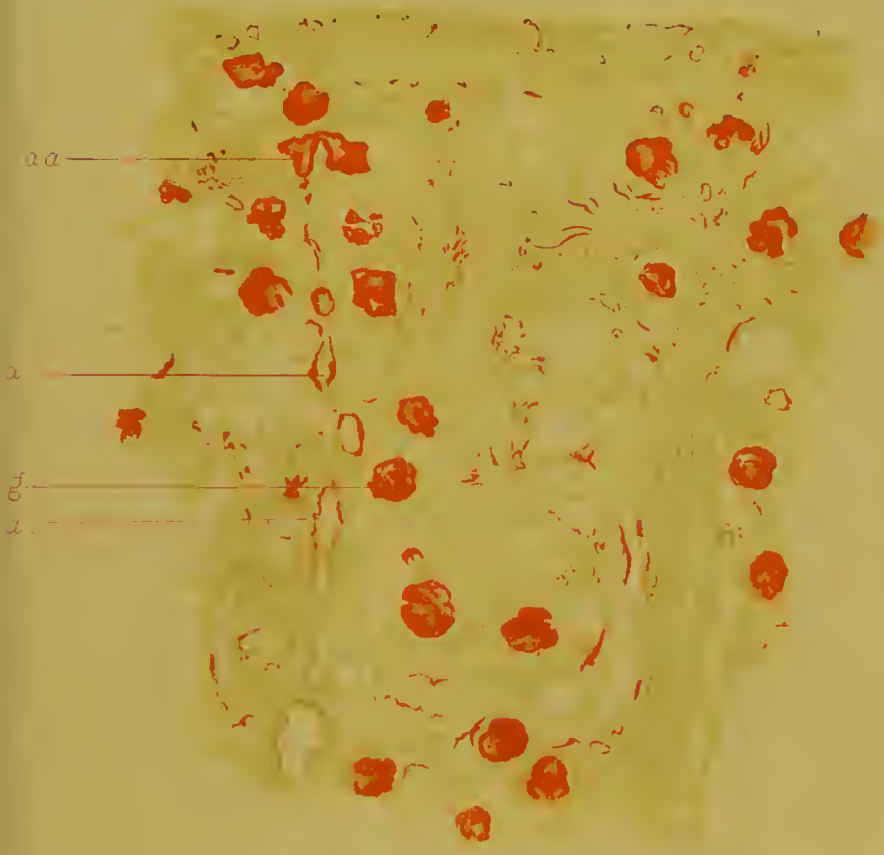


FIG. 52.—Drawing of a section of kidney with advanced waxy disease, complicated with interstitial nephritis; stained with methylaniline violet. (× 30.)

a.i. Interlobular artery, the walls of which are waxy.
g. Glomerular tuft, waxy.
a.a. Afferent arteriole.

The small waxy circles are basement membranes of tubules and small intertubular capillaries. For explanation of dense mass near the surface and along the lines of the interlobular arteries, with the more open tissue between, see section on Subacute Interstitial Nephritis (§ 167, p. 207).

in Farrant's solution (§ 98, p. 71), or acidulated glycerine (§ 93, p. 68).

Under the low power (× 50) observe how extensive the change is. In the Malpighian body the capillary tuft may be affected throughout, in which case the various patches of waxy disease run together. In the basement membrane of Bowman's capsule, and even in the flattened cells which line the capsule, a similar waxy deposit may take place. The interlobular and afferent arterioles are markedly affected, as are also the efferent arterioles and the interlobular capillary vessels. If a careful search be made in the basement membrane of the convoluted tubules, a similar change may be noted



FIG. 53.—Section of medulla of kidney, stained with iodine and sulphuric acid. (× 310. After Kyber.)

a. Straight tubule with colloid cast
c.c. in lumen.
b. Epithelium.
d. Shed epithelium, fatty and colloid.
e. Basement membrane; waxy (blue).
f. Descending limb of looped tube of Henle. Waxy basement membrane. Cells fatty.
g. Vessel, the walls of which are in an advanced stage of fatty degeneration.

here and there; but it is only in the rarest cases (if ever) that the epithelial cells become implicated in the waxy change. In this

epithelium fatty degeneration is a frequent condition, and when this condition occurs the cells become angular and have a shrivelled appearance. In a section treated with osmic acid numerous black globules and granules of fat are seen. The cells are badly nourished, and undergo fatty, but not waxy, degeneration.

In the medulla, from the boundary layer to the apices of the pyramids, the waxy change is in the walls of the vessels and the basement membrane of the straight tubules. It is always most marked in the muscular coat of the vessels; but in the later stages the intima may be involved, the endothelial lining of the vessel in such cases undergoing fatty degeneration. Nearer the tips of the papillæ, the connective tissue fibrils between the bundles of muscular fibres, which run from the tips of the papillæ for some distance towards the boundary layer, are affected, apparently quite apart from the vessels, and this change may occur where the other parts of the kidney are comparatively unaffected. The colloid casts are somewhat numerous throughout the whole section; they have been already described in the earlier stage. In the iodine stained section the affected parts are seen as mahogany brown patches when examined by reflected light, whilst the normal tissues appear yellow. With methylaniline violet, the waxy parts stain red violet, whilst the normal tissues, fatty cells, and colloid casts take on a blue violet or slaty blue stain.

Greenfield gives the order of affection of the various parts by the waxy change as follows:—(1.) Afferent arterioles; (2.) Groups of glomerular capillaries; (3.) Arteriolæ rectæ; (4.) Efferent arterioles, and the capillaries into which they break up; (5.) Capsule of Malpighian body; (6.) The capillaries which run between the bundles of straight tubes; (7.) The basement membrane of the convoluted tubules; (8.) Large interlobular arteries; (9.) Walls of the straight tubules, especially near the papillæ; (10.) Large branches of arteries and veins in the boundary area; (11.) The muscular or connective tissue around the collecting tubules at the tips of the papillæ; and (12.) The epithelial cells, rarely, if ever, affected.

Cloudy Swelling of the Parenchyma of the Kidney.

159. "Molecular," "Parenchymatous," or "Granular" degeneration is one of the first results of altered nutrition and function of the epithelial cells, especially of the convoluted tubules. It may occur as an early stage of an inflammatory condition of the epithelium, or it may simply be the precursor of fatty degeneration of the cells. The causes are much the same as the causes of the similar condition of the liver (§ 110, p. 82) and heart (§ 132, p. 132).

Naked eye characteristics.—The kidney is enlarged, the capsule strips off readily, the outer surface of the cortex has a peculiar shining opalescent appearance and pink colour. On examining a section of the kidney, the cortex is seen to be enlarged and pale, and the Malpighian bodies stand out prominently. The medullary rays are distinctly seen, and the pyramids are rather deep in colour. The vessels in the boundary area appear to be filled with blood; otherwise the boundary and papillary layers are normal in appearance.

Harden a very thin piece of this kidney in chromate of ammonia (§ 59, p. 45), and other pieces in Müller's fluid (§ 53, p. 42). Spirit alters the appearances of the cells, therefore should not be used as a hardening fluid for this tissue. Stain a section in picro-carmine (§ 73, p. 53), and mount in Farrant's solution (§ 98, p. 71).

Under the low power (× 50) examine the cortex, in which the principal changes are found. The sections of the convoluted tubules present a greater surface than in the normal condition. The lumen of the tube is very irregular in shape, and often appears to be little more than a stellate fissure. The epithelial cells can be recognised as having their outlines more distinctly marked and their diameter considerably increased.

With the high power (× 300) the epithelial cells are seen to be very greatly enlarged. They are angular, and project into the lumen of the tubule, so that sometimes, as previously observed, the lumen is almost obliterated. The outlines of the cells stand out very prominently; the protoplasm is extremely granular looking, much more so than in the normal condition, and the nucleus is obscured, though in a few cases the nucleus takes on the carmine stain very deeply, and thus may become more prominent than in the normal condition. Treat a

section with acetic acid (§ 93, p. 68) or caustic potash (§ 66, p. 47); the cloudiness disappears, and with the exception of the change in size and shape, the epithelium regains its normal appearance.

If the change has been going on for several days, a few clear highly refractile globules may be seen in the swollen cell, and the nucleus is almost obscured. (Treat such a section with osmic acid (§ 80, p. 62), when the globules are seen to take on the peculiar black reaction of fatty material.) Here the cloudy swelling is being superseded by fatty degeneration, a condition which the observer will meet in all cases of acute Bright's disease.

Under this power note that the interlobular capillaries appear to be somewhat compressed, and around them a few leucocytes have frequently escaped. The leucocytes take on the carmine stain very deeply. In the medulla the vessels are more distended, and there is frequently slight catarrh of the straight tubules, but no other change.

Simple Fatty Degeneration of the Kidney.

160. This may follow the above form directly, so that any cause of cloudy swelling may act as the causal agent in bringing about this condition. It is met with especially in patients who have succumbed to wasting diseases, such as cancer, phthisis, pernicious anæmia, Addison's disease, and diabetes, or to certain poisons, such as alcohol, sulphuric ether, phosphorus, arsenic, or antimony.

The naked eye appearances may or may not be characteristic, according to the stage of the degeneration. The kidney in the later stages is usually slightly smaller and paler than normal. The capsule strips off readily. On section, the cortex may be slightly wasted, mottled, and somewhat yellow. On the yellow background the interlobular arteries with their double rows of Malpighian bodies stand out prominently, giving the cortex a distinctly striated appearance (in phosphorus poisoning there may be small punctiform hæmorrhages in this position), and the striation in the medulla is also well marked; the tissue is flabby and greasy feeling.

Stain a section with osmic acid (§ 80, p. 62), and then with carmine (§ 75, p. 58); mount in Farrant's solution (§ 98, p. 71). Examine under a low power (× 50). In the convoluted tubules

the epithelial cells are swollen and contain droplets of fat (stained black with the osmic acid) of various sizes; but it is to be noticed that in the majority of cases these black droplets are found principally at the bases of the cells, or near the basement membrane and blood-vessels. Similar black dots are seen in the Malpighian bodies; these appear to be in the epithelium lining Bowman's capsule. In the straight tubules the fatty change is not so well marked, but the globules are scattered indiscriminately through the substance of the cell, and the collecting tubules are usually unaffected.

Under a high power (× 300) the ring of dark globules at the periphery of the tubule is seen more distinctly. It is composed of fat droplets of various size, some occupying a considerable portion of the cell, others being simply embedded in the surrounding protoplasm. The nuclei in such cells are frequently almost lost. The cells are very unequally affected; a few being comparatively healthy. Make out the position of the granules in the epithelium lining Bowman's capsule. In the straight tubules the fat droplets are distributed irregularly throughout the protoplasm of the cell.

In metallic poisoning the fatty degeneration is much more marked, the whole of the protoplasm of the various cells may become fatty, not only in the tubule, but also in the capillaries and connective tissue; in such cases small patches of blood corpuscles are met with as interstitial hæmorrhages, or as hæmorrhages into Bowman's capsule, or into the tubules. In many forms of this disease the degeneration is accompanied by fatty infiltration of the cells. As evidence of this note the position of the fat globules, especially at the bases of the epithelial cells in the secreting or convoluted tubules. Treat sections with caustic potash (§ 66, p. 47) and with acetic acid (§ 93, p. 68). The fat is entirely unaffected, and the nuclei have undergone the fatty degenerative changes.

Kidney of "Acute Parenchymatous" Nephritis, or Kidney of "Acute Bright's Disease."—Acute "Desquamative," "Tubular," or "Catarrhal" Nephritis.

161. Of these names the first is undoubtedly the best, as it refers rather to the physical conditions than to any theory as to the processes which take place during the course of the disease.

It is found in patients who during life passed albuminous and smoky urine, containing hyaline, and blood casts, &c. Causes,—sudden congestion, and overwork of the kidneys, febrile conditions, pneumonia, and similar diseases. The earliest condition has been described as cloudy swelling of the epithelium of the kidney.

In the following stage of early but well pronounced acute Bright's disease the naked eye characteristics are—the kidney is flabby and considerably increased in size, especially in thickness, so that the organ is more rounded; the capsule is tense, but strips off even more readily than in the natural condition from the surface, which is slightly œdematous in appearance; the outer surface is pale and has a peculiar mottled appearance, and on this pale background the venæ stellatæ stand out prominently; there are usually no cysts present; on section the cortex presents the same peculiar mottled and granular appearance. It is both relatively and absolutely much increased in thickness, and although large quantities of blood escape from the cut vessels, the cortex is pale when the blood is washed away, but on the pale pink background are "opaque pinkish points" and "markedly injected dots, due to the swollen vessels and glomeruli." If the process is very acute, small hæmorrhages are found in the cortex, and the whole of the cortex may be intensely injected and red. The medullary portion of the kidney is simply congested, and rarely takes part in the graver changes at this stage. The mucous membrane of the pelvis of the kidney is much injected.

Harden a piece of this organ in Müller's fluid (§ 53, p. 42), cut sections (§ 67, p. 48), stain one in picro-carmine (§ 73, p. 53), and a second in osmic acid (§ 80, p. 62). Mount both in Farrant's solution (§ 98, p. 71).

Examine under a low power (× 50). In a few of the convoluted tubules the cells are in a condition already described as cloudy swelling. In others the cells are evidently undergoing rapid proliferation, and the large swollen cells are dividing. In these dividing cells evidence of degenerative change may be observed, the swollen protoplasm is granular, and in many cases this is so marked that the epithelium is quite opaque and the nuclei are obscured. In the opaque masses of protoplasm small oil droplets are frequently seen, especially if stained with osmic acid. Blocking up some of the tubes

are masses of broken down fatty cells, which, accumulating, form a kind of plug. These changes are confined to the tubules in which the epithelium is columnar, hence they are seen only in the cortex and part of the boundary area. The interlobular vessels and afferent arterioles are distended, and the Malpighian bodies appear to be considerably increased in size, from the larger quantity of blood which is contained in their capillaries. Around the glomerular capsule a number of small pink dots are seen, more of them than is usual. These are leucocytes and nuclei of young connective tissue cells. There are quite sufficient of these to point to the fact that along with the parenchymatous inflammation there is even at this early stage of the disease some interstitial change. In some of the Malpighian bodies, and in or around some of the convoluted tubules, masses of blood corpuscles are present which have passed out from the vessels ruptured by the high blood pressure. A mass of brown pigment in some cases is all that is left to represent the blood, especially in the straight tubules. Tube casts (hyaline, blood, and a few fatty casts) are met with at this stage in the convoluted tubules, and also in smaller numbers in the straight tubules, whither they have been washed down. The vessels in the medulla are filled with blood.

Under the high power (× 300) all the above conditions are more readily recognised. The congestion of the vessels in both cortex and medulla, the crimson nuclei around the Malpighian bodies, the swollen, extremely granular or proliferating and slightly fatty cells in the convoluted tubules and ascending tubule of Henle, the casts of various forms—hyaline, seen as very transparent material, fatty casts, in which the outlines of the cells may still be made out—and the blood casts or masses of altered blood in the convoluted and straight tubules.

Large Pale Kidney.

162. A more advanced stage of this form of Bright's disease is that spoken of as the "Large Pale" or "Fatty" Kidney. These are both faulty names for this condition, as the waxy kidney is also sometimes spoken of as the large pale kidney, as is also the kidney of subacute interstitial nephritis, which is even paler than the advanced parenchy-

matous form, and the fatty change in the epithelium is common to this and to many other forms of disease. Of the two names, however, the latter is preferable.

To the naked eye this condition is characterised by considerable enlargement. The capsule is still readily separable. The outer surface of the cortex is pale and mottled looking, and the organ is considerably less vascular than the normal. On section, the cortex is swollen, and has a mottled pink and yellow surface. The Malpighian bodies are not more prominent than usual. On scraping the surface, fatty streaks are seen floating in the fluid. In the medulla the congestion has disappeared, as also from the pelvis of the kidney. Harden a piece of the organ in Müller's fluid (§ 53, p. 42), cut sections (§ 67, p. 48), stain one in osmic acid (§ 80, p. 62), a second in picro-carmine (§ 73, p. 53), and mount both in Farrant's solution (§ 98, p. 71).

Under the low power (× 50), in the osmic acid stained section there is a quantity of black material in the convoluted tubules. This is simply the fattily degenerated epithelium already referred to. The vascularity between the tubules is not great, but the nuclei around the Malpighian bodies have increased in number. Some of the tubules are comparatively open, and appear to be lined by a layer of flattened cells, and even in those which are choked with the blackened epithelium the flattened cells may be seen lining the tubule. Around the tubules nuclei similar to those seen around the Malpighian body are met with. The casts in the tubules are more colloid and fatty than in the earlier stages of the disease. They are especially numerous in the lower part of the convoluted tubules, and in the first part of the straight tubules.

Under the high power (× 300), the epithelium lining the convoluted tubules is flattened, and forms a thin cellular layer around the lumen of the tubule, or the mass of fatty material occupying the lumen. These flattened cells are young epithelium. They take on the carmine staining very readily, and are not granular or fatty. The cells, or the *débris* of cells forming the tube casts, are stained yellow. Verify the other conditions seen under the low power, more especially the cellular increase around the Malpighian bodies and around the tubules. Look for dilated tubules blocked up at points by the tube

casts. Complete desquamation does not take place, a thin layer of cells always remaining, which after a time grows, and reproduces the epithelium more or less perfectly.

In the straight tubules the cells may also present this flattened appearance, and casts of small cells are frequently met with in this situation.

Scarlatinal Nephritis.

In scarlet fever, nephritis is an extremely common condition, and from this fact certain forms have been described as occurring especially in this disease. Of these, two are described below as fairly typical cases.

Acute Scarlatinal Nephritis.

163. Scarlatinal nephritis fatal at the end of the first week after the onset of the fever, convulsions and death following suppression of urine. To the naked eye the organ is somewhat like the kidney in cloudy swelling, but it is more congested, whilst at the bases of the pyramids, and scattered through the cortex, are small hæmorrhagic patches. The positions of the Malpighian bodies are also readily distinguished in this condition. In some cases, however, it must be remembered that the kidney may, with the exception of some hyperæmia, appear perfectly normal.

Harden a piece of the kidney in Müller's fluid (§ 53, p. 42), and another piece in absolute alcohol (§ 51, p. 42), stain a couple of sections in carmine (§ 75, p. 58), mount one in Farrant's solution (§ 98, p. 71), and the other in Canada balsam (§ 96, p. 69).

Under the low power (× 50) the most marked changes are seen to be around the interlobular arteries. Examine these at their origin in the boundary layer and as they pass outwards to the cortical surface; around each of them are deeply stained granular-looking patches, which follow the lines of the afferent arterioles. They also occur around the Malpighian bodies. Extending from them for some distance between the tubules are similar granular looking patches. Beneath the capsule and around the terminal branches of the interlobular arteries are wedge-shaped patches of the granular material, the

base of the wedge being towards the cortical surface. Near the medulla this mass is also somewhat wedge-shaped, but in this instance the apex runs upwards to meet the apex of the mass at the surface. The vessels in these patches are very prominent. Around the glomerular tuft, forming a kind of bounding line between the tuft and the enormous mass of granular material, Bowman's capsule is seen as a distinct hyaline translucent layer, within which numerous small pink dots are seen. At the point where the afferent arteriole enters the thickened Bowman's capsule there is frequently some thickening of the vessel. The tubules are filled with epithelium in a most typical condition of cloudy swelling; the cells are large, angular, projecting, and distinctly outlined; the lumen of the tubule is exceedingly small and irregular in shape, and even under this power the cells appear cloudy and opaque.

Examine under the high power (× 400).

Changes in the walls of the vessels.—The interlobular arteries and the arterioles stand out more prominently than in a normal kidney. Their transverse diameter is increased, which increase is especially well marked at the points where branches are given off, and near Bowman's capsule, and is said to be due to two factors—(1) hyaline swelling of the intima, which takes place irregularly along the course of the vessel; (2) an infiltration of the muscular coat with nuclei, and consequent thickening: this takes place especially near the entrance of the arteriole to Malpighian body. Klein describes emboli in these positions, but although I have no doubt as to their existence, I have as yet been unable to verify the observation.

Changes around and in connection with the vessels.—The distribution of certain pink granular material was followed out under the low power. If a patch of the pink granules be now examined, it will be seen to be composed of small round cells which have all the appearances of leucocytes. Some of these cells are undoubtedly exuded from the blood-vessels, for alongside them are found numerous coloured blood corpuscles; it is probable, however, that some of them are young connective tissue corpuscles, derived by proliferation from pre-existing connective tissue cells. This exudation should be observed around the glomeruli, and also running in between the tubules around them.

Changes in the glomeruli.—These are, as already seen, usually enlarged, and appear to be more deeply stained than is normally the case. The capillaries forming the tufts are swollen, whilst the inter-

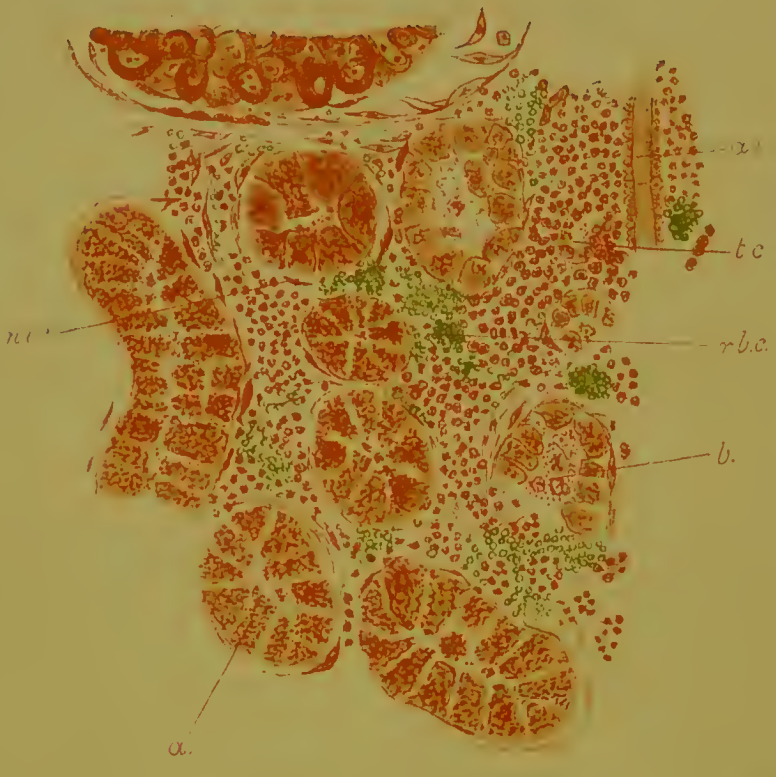


FIG. 54.—Acute scarlatinal nephritis; death on eighth day. Section stained with carmine, and mounted in Farrant's solution. (× 300.)

a. Epithelium in an advanced state of cloudy swelling.
b. Commencing catarrh in the tubule, cells proliferating, some detached from the deeper cells, which are more or less flattened.
a.i. Interlobular artery, around which is a great amount of round cell infiltration.
r.b.c. Coloured blood corpuscles.
t.c. Section of atrophied tubule, compressed by the round celled exudation.
n.i.c. Nuclei of intertubular capillaries, near which the round cell infiltration is also well marked.

capillary nuclei or the nuclei of the supporting connective tissue are increased in number. These nuclei, however, are similar in all respects to those seen outside the glomeruli, and many, therefore, are probably exuded leucocytes resulting from the acute inflammatory process.

The basement membrane, or Bowman's capsule proper, is considerably thickened, and appears to be homogeneous in structure. At

this stage cloudy swelling and even proliferation of the flattened cells lining Bowman's capsule is frequently seen.

The changes in the tubules are exactly those of cloudy swelling and slight catarrh, and have already been described (§ 159, p. 190). In some of the tubules gelatinous and blood casts are sometimes, but by no means invariably, met with.

If the above conditions be looked upon as occurring in a less acute, and gradually merging into a more chronic, form, the other conditions of scarlatinal kidney will be much more readily understood. The changes which appear to be of the greatest importance are those which take place in the vessels and glomeruli, but they are accompanied or followed by secondary changes in the epithelium.

Scarlet Fever Kidney (No. 2).

169. Found in cases where death has taken place at from the seventh to the fourteenth week of the disease.

In this condition the organ may be even smaller than normal, or only slightly enlarged. It is tough and dense; the capsule is readily removed, leaving the surface of the cortex pale or of a "pinkish colour, and more translucent than natural, on which the angular glomeruli may frequently be seen as brownish red dots." (It will be remembered that in the normal kidney the glomeruli are never seen on the surface.)

On section the cortical substance may be present in almost its normal proportions, but more frequently it is considerably narrowed. The interpyramidal cortex, on the other hand, is usually swollen, in some cases markedly so; it is of "opaque yellowish or pinkish white colour, mottled with opaque yellowish white points." This increased size of the interpyramidal cortex frequently gives rise to compression of the bases of the pyramids, which do not stand out so prominently as usual.

The superficial cortex on section is of much the same colour as is the surface, and the parallel rows of enlarged glomeruli are usually distinctly seen on each side of the prominent interlobular artery. Some of the glomeruli appear as translucent greyish spots, whilst others appear as brownish red angular bodies. Where the brownish

red masses are seen, patches of inflammatory exudation will be found surrounding the glomeruli. There are also angular yellowish patches, which represent to the naked eye the fatty and degenerative changes taking place in the epithelium of the convoluted tubules of the cortex. The medulla presents a comparatively normal appearance, with the exception of the bases of the pyramids.

Harden a piece of the kidney in Müller's fluid (§ 53, p. 42), and a second piece in absolute alcohol (§ 51, p. 42), cut sections (§ 67, p. 48), stain one in picro-carmine (§ 73, p. 53), and mount in Farrant's solution (§ 98, p. 71). Stain another in logwood (§ 74, p. 57), and mount in Canada balsam (§ 96, p. 69).

Examine especially the Malpighian tuft around or in which the principal changes are taking place. Along the course of the afferent arterioles, and even along the interlobular arteries, there is frequently some increase in the number of pink-stained nuclei, pointing to an increase in the amount of connective tissue; but when the Malpighian body is reached, there is frequently an enormous mass of the small pink points around the capsule. These are also seen running in between the tubules in the immediate neighbourhood, just as in the very acute form already examined. Within the capsule the number of nuclei is also increased, and the vascular tuft may appear to be diminished in size. Some only of the Malpighian bodies are affected in this condition, and they are affected very irregularly. The convoluted tubules immediately around the Malpighian bodies appear to be compressed by the inflammatory growth around them, and marked catarrhal changes may also be observed in them. The cells lining the tubules are flattened, whilst in the lumen small granular masses may be seen even under this power.

Some of the convoluted tubules, and some of the straight tubules also, are choked with broken down fatty catarrhal cells.

Under the high power (× 300) the swelling of the intima described as occurring in the acute stage may also be distinguished in this form in the interlobular and afferent arterioles. The nuclei surrounding the vessels belong to the cells of inflammatory origin, and in many cases are in process of organisation into more or less highly developed connective tissue. Similar cells are present in great numbers around the Malpighian bodies, and radiating from them to the interlobular

fissures, or along the lines of the intertubular capillaries. Bowman's capsule is swollen and hyaline, though in the later stages it may become laminated. Within the capsule there seems to be an increase first in size and then in number of the flattened cells lining it, and within this again there is proliferation of the connective tissue cells supporting the capillaries. In consequence of these changes, and of the partial organisation of the young cells, the glomerular tuft affected may become much smaller and atrophied. The tubules near the Malpighian bodies are atrophied or compressed, the epithelium is flattened, whilst, as seen under the low power, there is in some of the straight and of the convoluted tubules an accumulation of catarrhal cells, forming the so-called fatty and granular casts. Along with the above conditions there is frequently simple catarrh in the straight collecting tubules. In this form the atrophy of the superficial cortex is said to be due to the obstruction of the arterial system. (See condition of the vessels, § 163, p. 197.)

Scarlet Fever Kidney (No. 3).

165. Found in patients who succumb to this disease during the first seven to fourteen weeks, the symptoms during life being the passage of scanty albuminous urine, accompanied by marked dropsy. Its naked eye appearances are very similar to those met with in the second stage of acute parenchymatous nephritis. It is one of the so-called large pale kidneys, the two kidneys together weighing from fourteen to sixteen ounces. The enlarged kidney may be rounded, stretching the capsule, which strips off readily. The cortex is smooth, and mottled yellow on a pale background, and the venæ stellatæ are distinctly marked. On section, the cortex is enormously thickened, and the Malpighian bodies are seen to be enlarged (they are often three or four times as large as normal) and angular, but regularly arranged in parallel lines running from the boundary layer to the cortical surface.

Harden a piece of the kidney in Müller's fluid (§ 53, p. 42), cut sections (§ 67, p. 48), stain one in picro-carmine (§ 73, p. 53), and a second in logwood (§ 74, p. 57).

Examine under a low power (× 50), and note that all the condi-

tions of acute interstitial and glomerular nephritis may be observed. The appearances are similar to those described above, except that the whole of the Malpighian bodies appear to be affected, and that between the convoluted tubules there is a most extraordinary increase in the amount of young cellular connective tissue. In consequence of this the tubules are atrophied and widely separated, and the epithelium within them is in a state of marked proliferation and catarrh. Fatty casts may be seen in both convoluted and straight tubules.

Under a high power (× 300) examine more carefully for the changes which have taken place in the Malpighian bodies. The epithelium lining Bowman's capsule is in an advanced stage of proliferation, and forms a layer which by its increase in size exerts a marked pressure on the glomerular tuft. At the same time there is an increase in the amount of connective tissue between the capillaries, and the cells on the surface of the tuft are also said to multiply and pass inward between the vessels, in this way gradually compressing them.

The endothelioid cells, by their proliferation, form a laminated structure, said by some to become organised into true fibrous tissue, and undoubtedly in many cases there is evidently a fibrous tissue formation in the later stages of the disease. Under this power there is also seen the periglomerular inflammatory new formation, partly from exudation, and partly from proliferation of the connective tissue cells. This new formation, in a number of cases, extends between the tubules, and is met by a similar new tissue formation along the lines of the whole of the intertubular capillaries. It is composed of deeply stained rounded or slightly elongated cells, with here and there a few spindle shaped or even branched cells, with a delicate fibrillar tissue between them, stained very slightly with the carmine of the picro-carmine. The tubules are widely separated by this tissue, and are undergoing atrophic changes; they are considerably narrowed, and their epithelium is usually flattened, though in some cases it appears to be swollen as in cloudy swelling, or more frequently it is undergoing division, and a number of proliferated or catarrhal cells are thrown off into the lumen of the tubule. These catarrhal cells are fatty, and form the greater part of the tube casts to which reference has already been made (§ 161, p. 194).

The great increase in the size of the kidney appears to be due to the enormous exudation or new formation of cells in the glomeruli and between the tubules of the cortex.

The more chronic forms of this scarlatinal nephritis are so like the following, that it is unnecessary to give a separate description, if the observer bear in mind that in the scarlatinal forms the glomerular changes predominate, whilst in the other forms the interstitia changes are usually more "diffuse."

Subacute Interstitial Nephritis,

Or the Large, Pale, Smooth Kidney following Acute Bright's Disease.

166. After the consideration of the above forms of disease of the kidney, the student will be in a position to understand the appearances in the more chronic forms of nephritis; and from the description given of the second stage of acute parenchymatous nephritis, he will be quite prepared to meet with considerable increase in the amount of connective tissue, especially between the convoluted tubules, at a still later period of the disease. The naked eye appearances of a kidney in such a condition are very similar to those already described in the third form of scarlatinal nephritis, except that the kidney is not so large, the cortex is not so thick, the Malpighian bodies are not so distinctly made out, and the tissue of the cortex is firmer, denser, and more translucent. There may be slight thickening and adhesion of the capsule, beneath which small cysts are sometimes met with in this form of disease, but not nearly so frequently as in the granular contracted kidney. There is frequently some congestion of the venæ stellatæ, and also at the bases of the pyramids.

In the boundary layer the arteries have rigid and thickened walls, and always remain patent and prominent.

Harden in Müller's fluid (§ 53, p. 42), make sections (§ 67, p. 48), stain one in picro-carmine (§ 73, p. 53), and a second in logwood (§ 74, p. 57). Examine a section under the low power (× 50). The Malpighian bodies have the normal arrangement, but they are in certain cases undergoing very great changes. These changes will be more readily understood if a general description of the appearances of the cortex is first given.

Commence the examination in the boundary layer, and notice that along the lines of the interlobular arteries there are wedge-shaped masses of solid looking tissue, the base of the wedge being directed towards the medulla. Dipping down from the surface is a similar wedge, the base here being situated at the cortical surface, the apex running down to meet the apex of the other pyramidal mass. Between the masses of more solid looking tissue are oval patches of comparatively normal and open kidney tissue. The open tissue is situated midway between the interlobular arteries, and consequently is composed of sections of straight tubules in the centre, of convoluted tubules at the margin. The convoluted tubules, especially near the margin of the denser tissue, are considerably dilated. In the denser mass are small openings lined with a layer of flattened fatty cells, which appear to be atrophied ; these are sections of compressed and atrophied convoluted tubules. Running fairly regularly along each side of the interlobular arteries are the Malpighian bodies, in some of which very decided changes have taken place, whilst others are apparently healthy. The healthy Malpighian bodies are almost invariably situated in the part of the kidney tissue which otherwise appears normal, *i.e.*, in the more open tissue. The Malpighian bodies which are situated between the open and denser tissue, or which are in only the margin of the denser mass, are very frequently somewhat increased in size owing to distension of the tuft along with an increase of the connective tissue within the capsule. Further in the denser wedge-shaped mass the Malpighian bodies are usually much diminished in size, and are more closely packed together. On a more minute examination of one of these the capsule is seen to be very much thickened and fibrous looking, and the glomerular tuft in many cases cannot be discerned at all, or only as a small knot of fibrous tissue. Between the atrophied tubules and the altered Malpighian bodies there is an enormous amount of small round-celled tissue, which in this case does not seem to affect the Malpighian bodies specially, but is distributed almost equally throughout the tissue along the lines of the interlobular and intertubular vessels. This small-celled material, as will be seen later, is probably young connective tissue, which tends to become organised, and it is this tissue which gives the dense appearance to the wedge-shaped masses. In the boundary layer the larger branches

of vessels are seen to have their walls thickened, and even under this power the thickening appears to be throughout the whole three coats. In consequence of this the lumen of each vessel is somewhat narrowed.

Examine under the high power (× 300), and observe first the condition of the Malpighian bodies. Within the capsule are found a number of layers of fibrous tissue, and within these layers are numerous cells. At other points the fibrous tissue may be absent, and there is simply the thickened layer of cells lining the capsule. Or, again, the thickening of the capsule may be exceedingly irregular. As already

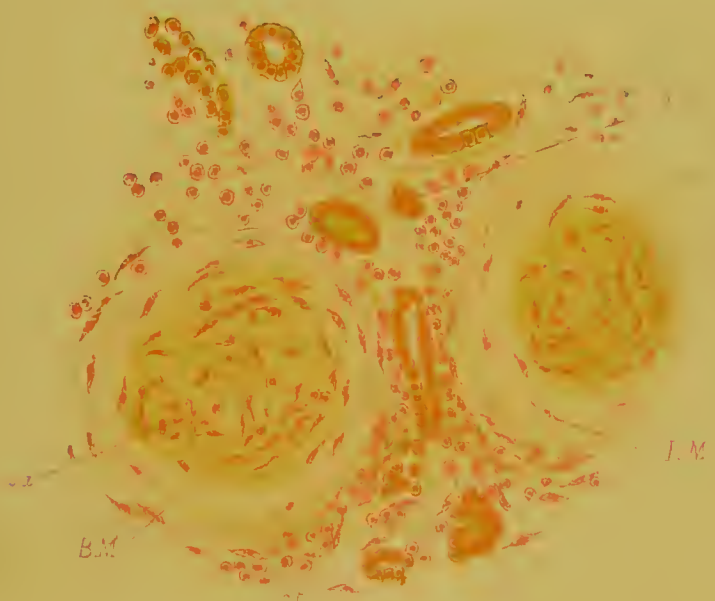


FIG. 55.—Section of a couple of fibroid Malpighian bodies from a case of subacute interstitial nephritis; section stained with picro-carmine and mounted in Farrant's solution. (× 300.)

B.M. Thickened Bowman's capsule, laminated and fibrous.
f.k. Central fibrous knot, which is all that is left to represent the capillary tuft.
a.a. Point of entrance of afferent arteriole.
a.t. Atrophied tubule, one of which at *c.c.* contains a cast rapidly becoming colloid.
c.t. Periglomerular new formation, tissue becoming fibrous. At certain points the tubules are not so much atrophied, and the epithelium is more natural in appearance.

seen, the thickening may be due to a growth by multiplication of the layers of cells within the capsule; or the capsule itself may be thickened by proliferation. Along with these conditions the peri-

glomerular infiltration is well marked, and there is also a rapid proliferation of the connective tissue corpuscles, which support and invest the glomerular capillaries. This may be so great, and the organisation of this tissue may be so far advanced, that the capillaries are atrophied by pressure, and nothing but a firm fibrous knot remains.

Changes in and around the Tubules.—The epithelium, though proliferating rapidly in the earlier stages of the disease, and forming irregular cells, does not desquamate ; for in carefully hardened sections a distinct epithelial layer is always present, which at first may be somewhat irregular in shape and size, but which, later in the course of the disease, becomes extremely flattened. Numerous fatty and colloid casts are found in the various parts of the convoluted and straight tubules.

Along the lines of the capillaries, and between them and the basement membrane of the tubules, numerous branching corpuscles are frequently seen. These are the more fully developed connective cells, of which so many have been seen in an undeveloped condition around the Malpighian bodies and the atrophied tubules; they form a firm fibrillated connective tissue. Secondary to this fibrous tissue formation the capillaries become atrophied, though the intertubular vessels still remain patent.

Changes in the Arteries and Arterioles.—The inner coat within the internal elastic laminæ is frequently thickened. (See Endarteritis Obliterans, § 149, p. 163.)

The muscular coat is hypertrophied, and along with the hypertrophy there is frequently an increase in the number of connective tissue nuclei in the media, though this seems to be a very variable condition.

As already noticed, there is a general increase in the interstitial connective tissue ; and the tunica adventitia of the arteries, which is really a part of, or is directly continuous with, the interstitial tissue, takes part in the general thickening.

It is held, with a considerable show of reason, by some authorities that this form of interstitial nephritis is but an early stage of the granular kidney, especially of the larger form ; and as the changes in that larger form are very similar to those above given, it will here be necessary to describe the small granular kidney only.

Chronic Interstitial Nephritis.

167. "Granular Contracted" Kidney, "Cirrhosis" of the Kidney, "Small Red" Kidney, "Gouty" Kidney.

Naked eye appearances of the small or typical form.—The kidney is very much diminished in size; it is tough, and feels like leather, and has been compared to a piece of thick moist leather. The capsule is thickened, opaque, and laminated, and is firmly adherent to the subjacent tissue, so that it comes away in layers, leaving shreds adherent to the kidney substance, or else bringing away with it fragments of the parenchyma. It leaves an extremely granular surface, which feels like a piece of moist morocco or shagreen, the granules being small, and fairly regular in size, and pale; the fossæ around them are usually injected, and much redder in colour than the elevated patches. Over the surface of the kidney are deeper and more irregular sulci, which divide the kidney into areas, sometimes corresponding accurately to the outlines of the lobes of which the organ is made up, but this is by no means a constant condition. In the cortex numerous cysts are found, varying very greatly in size, from almost miscroscopic cavities to others as large as a walnut, or even larger, and small brick red or yellow points are also seen scattered over the surface.

On section the cortex is found to be most markedly contracted, and may be only a sixth of the normal thickness; the thinning being most marked at the bases of the pyramids. The edge of the cut surface is sharply marked, but uneven, the elevations corresponding to the granules already described. The colour of this section varies very greatly, but in a very large proportion of cases it is of a brick red colour, and is not specially anæmic. Here, too, small cysts are seen, most of them filled with a yellow gelatinous material, and brick red or yellow lines are also seen scattered at irregular intervals over the surface of the cortex, similar straight lines appearing in the medulla. There are accumulations of urates in the tubules. In this section, notice further that the parallel radiating lines composed of the straight tubules and double rows of Malpighian bodies are either altogether obliterated, or they are tortuous and irregular, and that the interlobular arteries are tortuous and thickened. This irregularity

is extremely characteristic of this form of kidney, and even in the early stages of the disease, when no other naked eye sign of the atrophy is apparent, this is quite sufficient to indicate its presence. The large branches of the renal artery appear rigid and atheromatous, those in the boundary layer have their walls thickened, and the lumen very patent, so that they stand out much more prominently than in the normal kidney. Passing to the interpyramidal cortex, this is found to be pale, frequently swollen, and only atrophied in the very late stages of the disease. The medullary pyramids are usually somewhat atrophied, but present no marked naked eye changes. In the pelvis there is frequently more fat than usual around the calyces to which the fat along with the capsule is adherent.

Harden in Müller's fluid (§ 53, p. 42), make sections (§ 67, p. 48), stain one in picro-carmine (§ 73, p. 53), and a second in logwood (§ 74, p. 57).

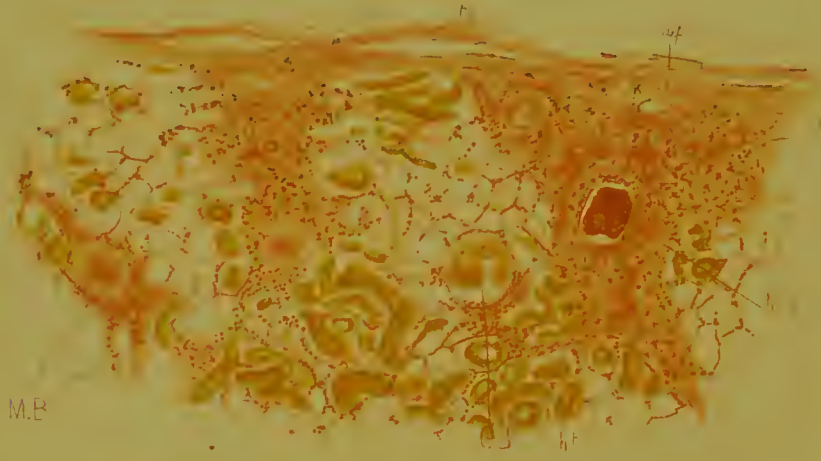


FIG. 56.—Part of cortex of granular contracted kidney stained with picro-carmine. (× 40.)

t.c. Thickened capsule, laminated and adherent.
w.p. Wedge-shaped patch, composed of atrophied tubules (*a.b.*) and fibroid Malpighian bodies (*M.B.*).
o.t. Ovoid patch of open tissue composed of dilated convoluted tubules, from which most of the epithelium has fallen out.
C.B. Enlarged Malpighian body, forming early stage of cyst, situated at the margin of the more solid patch.
l.t. Comparatively healthy tubules.

Examine under a low power (× 20), and notice that the free cortical surface is very irregular from elevations and depressions corresponding to the granules; and observe that the capsule is thickened and

laminated and stained pink with picro-carmine. Running from the depressions down along the lines of the interlobular arteries are wedge-shaped patches of dense granular looking tissue ; the base of the wedge situated towards the cortical surface. Between these dense masses are patches more or less oval, which are evidently composed, as in the case of the subacute interstitial nephritis, of sections of the straight and some of the convoluted tubules, either normal in size or greatly distended. It will be sufficient to describe one of these dense patches and one of the open networks along with the vessels in the boundary layer. Commencing at the centre of the patch, and working outwards, it will be noted that the centre is occupied by the interlobular artery, which is somewhat thickened and tortuous. Around this the Malpighian bodies appear to be massed closely and much more irregularly than in the normal condition. The Malpighian bodies nearer the surface of the kidney and nearer the centre of the mass are represented by only a yellowish dot, whilst those situated more deeply in the organ or nearer the margin of the dense mass are surrounded by thickened capsules and may be smaller than normal, or the atrophied tuft of vessels may be seen contained within a large cyst : the cyst in this case is formed of the distended and thickened Bowman's capsule. In the centre of small rounded masses of granular material, as seen under this power, are some very minute openings ; the granular material in which they are situated is not quite so opaque as that of the surrounding tissue. These are the atrophied convoluted tubules which are lined with flattened epithelial cells. The tubules in the open network are also, in some instances, distended and lined with flattened epithelial cells. The irregularity and tortuosity of the medullary rays as they pass to the surface are in great measure due to the unequal dilatation of some of these tubes, of course along with the contractions which take place in the fibroid patch.

Examine under the high power (× 300). The tissue of which the dense patch is composed is seen to be principally atrophied tubules and Malpighian bodies. Between these, however, there appears to be a slight increase of inflammatory connective tissue. In this form of the disease the inflammatory tissue is, according to the most recent researches, in great measure quite a secondary formation, and

one which follows the atrophy of the tubules. It is frequently exceedingly cellular or almost granular in appearance, even under the high power, and very little fully formed fibrous tissue is observable. In the mass of tissue the intertubular capillaries are frequently obliterated at points, but to make up for this, there is an accession of small branches from the capsule; these run into the mass at the most retracted parts, and appear to communicate with the terminal branches of the interlobular arteries. The Malpighian bodies, as already seen, present three distinct forms:—(1.) the pink ring composed of fibrous concentric laminæ, in the centre of which is the yellow atrophied knot of capillaries; (2.) the enormously thickened and fibrous capsule, with the capillary vessels of the tuft still patent; and (3.) the thickened and distended capsule, with the capillary tuft lying within, but only partly filling it. The method of formation of the thickened capsule has already been referred to.—(See Subacute Interstitial Nephritis, § 166, p. 204.) The tubules found in the dense mass are in various stages of atrophy. The lumen is small, the epithelium is flattened or irregular, and is undergoing fatty degeneration, whilst numerous colloid casts (stained yellow with picro-carmine) are seen in them. Casts of a similar nature are also found in some of the dilated tubules which form the open network. These tubules are lined by a flattened epithelium, which may or may not be undergoing fatty degeneration. On a careful examination of the larger arteries, it will be found that they are in a condition similar to that met with in subacute interstitial nephritis (§ 166, p. 206).

The great feature to notice in this condition is that it is an exceedingly chronic process, and appears to consist primarily of an atrophied condition of either the Malpighian bodies or the tubules, followed very gradually by a slight increase in the amount of connective tissue. It commences near the surface or around the terminal branches of the interlobular arteries, and gradually spreads down to the medulla, which may also become involved at a later stage. There is a so-called large granular kidney in which the process is preceded or accompanied by a considerable increase in the amount of connective tissue. This is more like the subacute interstitial nephritis, of which it is more than possible that it is the chronic continuation, more or less acute exacerbations occurring at intervals.

Cysts in the Kidney.

168. Cysts in the kidney may now be considered, as it is necessary to understand the method of their formation in order to arrive at a proper understanding of their significance as diagnostic features.

The true secondary cyst may be formed in one of three ways.

(1.) Distention of Bowman's capsule of the Malpighian body, owing to the obstruction of the narrow outlet or neck, frequently by a plug of colloid material, or more rarely by constricting fibrous bands. These cysts are seldom of large size, as the outflow of fluid from the capillary tuft ceases as soon as the pressure in the cyst equals that in the blood-vessels. The capillaries atrophy when their function is lost, and a cyst is left. These may be filled with watery material or with colloid material, derived from the degenerating epithelial cells.

(2.) Simple cysts in the tubules, formed in the same manner.

(3.) Rows of cysts where the convoluted or straight tubules become irregular, varicose, and tortuous, forming a chain of small cysts. They occur especially in the granular contracted form of kidney, and in the tubules which are situated near the margin of the wedge-shaped mass. Colloid plugs are formed at certain points, usually where there is already slight constriction from the pressure of fibrous bands; above this point there are other slight constrictions, and as the tube becomes distended it becomes so unequally, and a row of cysts is formed, the dilatations and constrictions alternating.

For cysts to grow there must be two factors at work—(1.) the watery secretion must be going on above the constricted point; and (2.) epithelium must be growing, must be shed, and then, undergoing degeneration, is washed by the urine until it eventually forms colloid material.

The contents of these cysts may be—

(1.) Serum, or the watery part of the blood with the salts. This occurs most commonly.

(2.) Colloid; a gelatinous, homogeneous material, derived from the degeneration of epithelium.

(3.) Urinous salts or urates, which are by no means uncommonly met with.

Cysts are most frequently found in connection with the various forms of interstitial nephritis.

Primary Cysts.—These are found in the so-called cystic degeneration proper. There are two forms—the congenital, and that which occurs during adult life.

In the first form, which occurs during fœtal life, the kidney may be enormously increased in size, or it may be smaller than normal. Both organs are affected. The cysts, which form the greater part of the organ, are probably distended tubules and glomeruli, the secretions of which cannot escape, owing to contraction of the afferent tubes in the atrophied papillæ. These cysts, unlike the other form, contain urinary fluid and salts.

The second form is very frequently unsuspected during life, and may give rise to no symptoms until late in life. Both kidneys are enlarged, and are converted into cysts, varying very much in size from that of a millet seed up to two-thirds of an inch, or even more. They contain albumen and blood pigment in various stages of alteration, so that they present all shades of colour, from yellow, through green and blue, up to purple. Cholesterin crystals are also met with, and in rare cases oxalate of lime and leucine—rarely any urinary salts. The fibrous cyst walls "are partially lined with flattened polygonal cells." It is quite possible that this may be the slowly growing or fully developed congenital form, but as yet little is known of the development of either of the two forms of cystic degeneration.

Tube Casts.

169. In the descriptions of the various forms of disease of the kidneys, various forms of casts have been already casually referred to, but it is necessary to consider these intratubular formations more systematically.

For the sake of convenience we may divide them into casts derived from (1.) hæmorrhages into the glomeruli or tubules; (2.) altered epithelium; (3.) urinary secretions; (4.) other materials not normally found in the tubules.

(1.) *Casts derived from Blood.*—Under the first form come the various *blood casts* which are met with in acute nephritis,

especially the scarlatinal form, in chronic venous congestion, or even in acute congestion of the kidney. In the acute diseases they are most frequently composed of but slightly altered red blood corpuscles, and are especially met with in the first part of the convoluted tubule. In the more chronic forms of disease they may be met with in this form, but they are also seen as pigment casts in the lower parts of the tubules, where they may be golden brown in colour, and are composed of hæmatoidin crystals or granules, or, in the straight tubules, of extremely black material, or melanin. In either case they are derived from blood pigment.

Hyaline fibrinous casts occur, especially in acute inflammatory conditions, but they may be met with even in health. They are usually seen in the looped and collecting tubules as delicate homogeneous casts, filling a considerable length of the tube. They are extremely difficult to recognise in an unstained specimen, but may be seen as very delicately stained homogeneous masses in carmine or logwood stained sections. They form the basis of a great number of other casts.

(2.) *Casts derived from Epithelium.*—The most common cast of this form is the *colloid cast*, a homogeneous, yellowish, translucent mass, found especially in the lower parts of the convoluted tubules in almost all cases of kidney disease where there are marked epithelial changes, as in waxy kidney, subacute and chronic interstitial nephritis, and such forms. In some cases the casts present the dim outlines of the cells of which they are composed, but most frequently they appear to be composed simply of a glue-like material, which gives a yellow reaction with picro-carmine, a brown waxy reaction with iodine, but a blue with methylaniline violet, so that it is not "waxy." They stain deeply with other reagents. They are usually surrounded by a layer of flattened epithelial cells, which appear to proliferate and add layer after layer of degenerated cells to the surface; consequently, the cast in some cases may present faint traces of lamination.

Granular casts.—Met with in the convoluted tubules in inflammatory conditions, or where marked atrophic changes are taking place in the epithelium. They are composed of a hyaline centre, with

granular protoplasmic material around, and are larger than the ordinary hyaline cast.

Fatty or oily casts are hyaline casts around which are fatty or albuminoid globules. (Not always fatty.)

Epithelial casts are usually found in the looped and straight tubules when these are in a condition of acute catarrh. Each has a hyaline basis, and is covered with a number of cells, derived either from the epithelium of the straight tubules or from exuded leucocytes.

Only those casts which are formed in the looped or straight collecting or excretory tubules come unchanged to the urine, but similar casts may be found in the upper parts of the tubules in sections of the kidney.

(3.) *Casts formed from Urinary Salts, &c.*—As seen in the case of the granular contracted kidney, crystals of acid urate of soda accumulate in the tubules of all the regions of the kidney, giving rise to the yellow patches mentioned under that disease.

Similar deposits of uric acid or urate of ammonia are frequently met with in the excretory tubes near the apices of the papillæ, in children who die within from two to fourteen days after birth, as "yellowish or brick-red lines," running from the apices for some distance towards the bases of the pyramids.

(4.) *Casts of foreign material.—Bilirubin casts* are dark granular casts, occurring chiefly in the straight tubules during the course of long-continued jaundice. They are probably closely allied to blood casts.

Calcareous casts are met with in the straight tubules in aged people, and in cases of osteomalacia, where there is a rapid absorption of the calcareous salts from bone. These salts are deposited as white masses in the excretory tubules near the apices of the papillæ. "They consist of dark, strongly refractile globules or nodular masses, which join together to form nodular rods." In a second form there is "an albuminoid basis, infiltrated with carbonate of lime." These stain deeply, but irregularly. On the addition of a weak acid they disappear, and carbon dioxide is given off. They are composed principally of carbonate of lime.

Tubercle of the Kidney.

170. This occurs as one of two forms:—(1.) Disseminated or miliary tuberculosis; or (2.) Tubercular pyelo-nephritis.

The disseminated form occurs most frequently as part of a general tuberculosis; in which case its affection of the kidney is, as a rule, late, and of comparatively little importance.

Naked eye characters.—The organ is not enlarged or markedly altered in any way. On stripping off the capsule and examining the cortical surface, small grey granulations, about the size of a millet seed, are seen projecting, very slightly, above the surrounding surface. On section into the organ these grey granulations are seen to be wedge-shaped, and to extend down into the cortex for some distance along the line of the interlobular artery. Similar masses may be more deeply situated in the cortex, when they assume an elongated or oval form; and deeper still in the boundary layer they are rounded. Nodules similar in appearance, but more translucent, are frequently found in the centre of the pyramids; but these are much firmer, and, on microscopic examination, are found to be composed of fibrous tissue. The small tubercle nodules are usually opaque, have a yellowish centre, and are rarely found in the medulla. Put some of this tissue aside to harden in absolute alcohol (§ 51, p. 42); and a second piece to harden in Müller's fluid (§ 53, p. 42); make sections (§ 67, p. 48); and stain one in picro-carmine (§ 73, p. 53); mount in Farrant's solution (§ 98, p. 71).

Examine under a low power (× 50). It is at once seen that the tubercular process is going on around the interlobular arteries. Each of the small opaque looking nodules is made up of several tubercle follicles, and around the nodules are evidences of the presence of an interstitial inflammation. The proper tubercular structure can rarely be made out, as in this organ caseation takes place at a very early stage of the process. Under this power, however, the cells—of which the various follicles are made up—may be seen to differ very considerably in size and structure. In the centre are numerous so-called endothelioid cells of irregular shape, each containing several nuclei, and frequently lying on extremely delicate filaments of pink tissue. Around are numerous

smaller cells, between which the pink fibrillated tissue is distinctly marked, especially at the outer part of the follicle, where it forms a kind of capsule. Usually small homogeneous or granular yellow patches may be seen in the centre of the follicle—this pointing to the fact that caseation is here commencing. Or the caseation may commence even earlier, when nothing is to be discerned but a mass of small rounded cells, with here and there a few of the larger endothelioid cells in the centre. In some few cases the typical giant cell formation (see Liver, § 123, p. 115) may be developed before caseation sets in; but in the kidney this is comparatively rarely met with. The softened points gradually increase in size, until several of them run together, and small cavities are formed; but this also is not of very frequent occurrence. Notice especially the arrangement of the tubercular nodules along the lines of the interlobular arteries, with their perivascular lymphatic sheaths.

Under the high power (× 300) the constituent elements of the tubercle follicle must be more carefully examined; the endothelioid cells of various shapes and sizes with several nuclei; between and supporting these cells the delicate fibrillar tissue; and at the periphery of the mass the small round cells with denser pink fibrous tissue between them. If there is a true giant cell system, the structure is the same as that in the liver. Note carefully that these tubercle masses have no vascular supply, the arteries becoming obstructed, and that the caseation takes place in the centre of the nodule, or in those follicles which are furthest removed from the blood-vessels at the periphery of the nodule.

Tubercular Pyelo-Nephritis.

171. Synonyms, "Genito-Urinary Phthisis," "Genito-Urinary Tuberculosis," "Scrofulous" or "Strumous Pyelitis," "Renal Phthisis" (not a good term), &c.

This disease of the kidney is usually associated with a similar condition in the ureter, the trigone of the bladder, vas deferens, vesiculæ seminales (scrofulous testicle). Both kidneys are then affected, but unequally.

In the fully developed disease the kidney is very much enlarged and lobulated looking, a marked depression existing between each projection; the projections vary in diameter from three-quarters of an inch to one and a quarter inches. The capsule usually strips off readily, and leaves a pale smooth surface, from which the venæ stellatæ stand out prominently. On cutting into the organ each of the nodules is found to correspond to a dilated—rounded or irregular—cavity, and each depression to a kind of septum—the septum corresponding in position to the interpyramidal cortex, and the cavities being situated where formerly the Malpighian pyramids were placed. Contained within the cavity is a yellowish or purulent looking fluid, in which caseous looking masses are found floating. The walls of the cavity are rough, and finely nodulated or papillated, or are ragged looking; they are lined by a soft, dirty yellow or caseous material, which may be readily removed with the finger-nail as a soft, putty-like mass. The pelvis of the kidney is lined by a similar material, and is usually considerably distended. The ureter, too, has its walls thickened, is blocked up with the same caseous stuff, and feels like a hard firm cord.

In the earlier stages of the disease small yellow caseous nodules, with small cavities in the centre, are situated towards the bases of the pyramids, and then extend upwards and downwards in the calyces and in the pelvis along the lines of the lymphatics in the submucous tissue. Ulceration following the caseation takes place along the lines already mentioned. Harden a piece of the wall of cavity in absolute alcohol (§ 51, p. 42); a second piece in Müller's fluid (§ 53, p. 42); stain a section in picro-carmine (§ 73, p. 53); and examine under low (× 50) and high (× 300) powers. The caseous material is stained yellow, and is composed of a mass of granular *débris*. Beneath this is a layer of tubercle follicles, which appear to undergo caseation at a very early period of development. Giant cells are rarely met with in the kidney; but if a piece of the tubercular testicle be examined, especially near the sinus, which frequently forms, giant cell systems are exceedingly numerous. The origin of this disease is as yet imperfectly understood; but it appears to be more than probable that there is a local tubercular process commencing in the mucous membrane, followed by early caseation and rapid ulceration; after

which the process may spread, either by the lymphatics or by direct infection. It is possible, however, that catarrh may be the first indication of the disease, and that this process is followed by a tubercular infection, giving rise to the above appearances and results.

Surgical Kidney.

172. Surgical kidney is a condition brought about very frequently in connection with stricture of the urethra, or renal or vesicular calculus, causing pyelitis or cystitis. It is also known by the following names :—" Disseminated Suppuration " of the Kidney, " Multiple Abscesses " of the Kidney, " Suppurative Pyelo-Nephritis."

Other causes of this condition are given, such as injuries, especially from blows, pyæmia, embolic abscesses, which occur during the course of ulcerative endocarditis, and similar conditions.

The kidney is usually irregularly swollen, though this is not necessarily the case; it is soft, flabby, and friable. The vascularity varies very considerably at different parts. On the surface small projecting yellow points may be seen surrounded by deeply injected or hyperæmic zones. On pricking these yellow points a small drop of pus escapes.

On section most of the yellow points are found to be in the cortex, where they assume a wedge shape, but a few elongated abscesses are also seen in the pyramids. Around each abscess the hyperæmic zone is well marked; where the condition is more advanced, the kidney may have the above characteristics exaggerated, whilst the small cavities have run together, and may occupy a considerable portion of the renal tissue. Where the abscesses are of considerable size they usually communicate with the pelvis of the organ, and contain urates mixed with the pus. Harden a piece of this kidney in absolute alcohol (§ 51, p. 42), cut sections (§ 67, p. 48), mount one stained with picro-carmine (§ 73, p. 53) in Farrant's solution, another must be stained with methylaniline violet (§ 76, p. 59), and mounted in Canada balsam (§ 96, p. 69).

Under a low power (× 50).—Examine first the cortex, in which may be seen a large quantity of granular material (deeply stained with the carmine) running along each side of the interlobular arteries

surrounding the Malpighian bodies, and also in between the convoluted tubules. This is most marked at the bases of the pyramids. From these points the granular material runs along the lines of the afferent arterioles, around the Malpighian bodies, and in between the tubules, which thus become widely separated from one another. Within the tubules the epithelium is granular, and appears to be undergoing a process of disintegration. Then observe that similar changes are taking place in the medullary portion of the kidney along the lines of the vasa recta, thence extending between the straight tubules. In some cases the changes are so grave that a mass of deeply stained granular material is all that is left of structure in these positions.

Under a high power (× 300) the granular material along the course of the vessels is seen to be composed of small round cells, which appear to be the products of inflammation; they cannot be distinguished from leucocytes or from pus corpuscles, and appear to be the result partly of inflammatory exudation, and partly of active proliferation of the connective tissue corpuscles. In many cases the cellular mass has fallen away from its position, leaving a small cavity, whilst in the more acute forms these cavities communicate with one another. Examine a section of the true surgical kidney stained with methylaniline violet, and note the small rod-shaped bacteria, which are very similar to those met with in decomposition products. Note, too, that these are principally in the tubules, the epithelium of which is undergoing marked fatty degenerative changes, but apparently there is no catarrh in these tubules.

In multiple abscesses resulting from septic embolic obstruction, in addition to the above appearances, masses of deeply stained micrococci may be found in the vessels (in a section stained with the methlyaniline violet).

Under certain conditions nephritic abscesses become more chronic, in which case large caseous masses may be met with, encapsuled by firm fibrous tissue. On microscopic examination, the tissue around is found to be atrophied, whilst chronic interstitial inflammatory changes are also met with.—(See Interstitial Nephritis, § 166, p. 203, *et seq.*)

Dilatation of the Pelvis and Calyces of the Kidney.

173. These may be due (1.) to tubercular thickening of the walls of the ureter; (2.) to obstruction of the ureter during the course of abscess of the kidney. This may be due (*a.*) to the presence of a calculus in the ureter,[1] or (*b.*) to the existence of some obstruction to the outflow of the urine from the bladder, accompanied or followed by decomposition of the urine in the bladder (stricture, enlarged prostate, and the rest). (3.) Simple obstruction of the ureter, or of its orifice, or of the outlet from the bladder, by any of the above agencies, without the decomposition of the urine in the bladder. These conditions give rise to simple hydro-nephrosis. Here the papillæ are the parts which become atrophied by the pressure of the urine as it accumulates, so that it is possible for them to disappear and leave the interpyramidal cortex projecting to form septa.—(See Tubercular Pyelo-Nephritis, § 171, p. 217.) The kidney presents a lobed external surface. Running down from the depressions are septa, more or less perfect, composed of membranous looking tissue. The cortex may be extremely thin and atrophied, and nothing but a thin crust may remain enclosing cavities of considerable size, which are filled with water and urinous salts. It is stated that if the disease is of long standing a mucous fluid only is found in these cavities.

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[1] Forms of Renal Calculi—

(1.) Reddish or brownish yellow uric acid calculi, in the form of gravel or rounded smooth masses, the size of a pea, or larger. These occur in great numbers.

(2.) Calculi filling the pelvis and calyces of the kidney, irregular and branching, with a somewhat rough surface, and composed of phosphates and uric acid or urates.

(3.) Oxalate of lime calculi, small, smooth, or mulberry masses, dark grey or purple in colour, and extremely hard. Soluble in the mineral acids.

(4.) Cystine calculi are rarely met with. They are light yellow, ovoid, crystaline masses; soluble in ammonia. From this solution the crystals may be obtained, by evaporation, in the form of hexagonal plates.

(5.) Xanthine calculi are also occasionally, but very rarely met with, as white waxy looking masses. They are soluble in hot nitric acid. When the solution is evaporated and the residue heated with caustic potash, "a beautiful violet red colour" is obtained.

Rarer Diseased Conditions of the Kidney.

174. *Syphilitic gummata* are extremely rare. They are situated near the surface of the cortex, are of small size, and present all the characters of gummata in other organs.

Leucocythemia.—Changes are sometimes met with in the kidney in this general condition. Both kidneys are affected. The cortex is pale and enlarged, with small hæmorrhages at intervals. A few larger hæmorrhages are met with in some cases. The medullary pyramids are pink, with similar hæmorrhages, usually situated at their bases. Harden in Müller's fluid (§ 53, p. 42), stain a section with logwood (§ 74, p. 57), mount in Canada balsam (§ 96, p. 69), and examine under a low power (× 50). Along the lines of intertubular capillaries, and within Bowman's capsule, there is an enormous increase in the number of stained nuclei.

Under the high power (× 300) these stained bodies are seen to be leucocytes, which have accumulated in enormous numbers in and around the intertubular capillaries and the capillaries of the glomerular tuft. With them are found numerous red corpuscles, which have escaped along with them from the ruptured vessels.

Examine one of the so-called hæmorrhages, and observe that it is also composed very largely of leucocytes. The epithelium in the tubules is comparatively healthy.

Tumours.

175. *Lymphadenoma* of kidney. — (See Lymphadenoma under Tumours.)

Fibroma of the kidney has already been described as a firm hard nodule, somewhat rounded or elongated in form, situated usually about the centre of the pyramids. (For microscopic appearances see section on Tumours.)

Muscular tumours—Myomata—are also found in this organ.

Cancer of the kidney, as a *secondary* formation, is somewhat frequently met with, principally as small nodules situated in the cortex. In this position, too, the malignant adenoma is found.

Where *primary*, the whole organ appears to become infiltrated, and may attain an enormous size. The tissue, examined microscopically,

very closely resembles the malignant adenoma already mentioned. (See section on Tumours.)

It is probable, however, that cancer of the kidney is by no means so common a condition as was formerly supposed, and that many so-called cancers are in fact sarcomatous growths.

Sarcoma.—In the secondary form the sarcomatous growths may attain a considerable size, and are to be recognised by their pulpy appearance and numerous hæmorrhages.

A primary form met with in children, leading to enormous enlargement of the organ, is usually lympho-sarcoma, or small round-celled sarcoma. In this, also, hæmorrhages are numerous.

Parasites.

176. (1.) Hydatid cysts are met with, though comparatively rarely in this organ.

(2.) In the mucous membrane of the pelvis of the kidney, the matured *Bilharzia hæmatobium* is sometimes met with, in which cases the ova may always be discovered in the urine.

(3.) The *Filaria sanguinis hominis* is met with in the kidney, and has been found in the urine during life in cases of chyluria.

(4.) A few instances of the presence of other parasites in the kidney, such as *Strongylus gigas* and *Pentastoma denticulatum*, have been recorded, but these are extremely rare. (See section on Parasites.)

Infarction in the Kidney.

177. Embolic infarcts may be met with in all stages of development, from the swollen, red, conical, or wedge-shaped patch in the cortex, or the dense, pale veined area, surrounded by a hyperæmic zone, to the caseous mass or cyst, surrounded by a fibrous capsule, or the simple, puckered, and retracted scar which marks the position of the old infarction. The description of an embolic infarct will be given in the section on Diseases of the Spleen, to which the reader is referred, as the process is essentially the same in all organs.

CHAPTER VII.

THE LUNG.

178. In order to thoroughly understand the various morbid processes in the lung, and to interpret aright the appearances presented by the tissues of the lung in certain diseases, it will be necessary first to examine the healthy organ, and to describe roughly its structure, reserving a description of special points in its histology to be given with that of the disease with which these points are more especially connected.

Naked eye appearances.—The lung, when taken from the body in the normal condition, should weigh about one lb. It is covered by, or contained within, a fibrous capsule, the outer surface of which is smooth, glistening, and serous. In people who live in the country, the lung often has a pink colour (Shetlander's lung), and this is the normal condition ; but in the lungs taken from the inhabitants of towns the pink colour is lost, and is replaced by a dull bluish or pinkish grey, with a series of darker streaks outlining the lobules. Such a lung crepitates under the finger. When a section is made, a quantity of blood, mixed with air, may be squeezed out ; but it is to be remembered that when the section is first made the bright arterial red colour is not observed (though this makes its appearance when the cut surface is exposed to the air for a short time), but a bluish purple. The bronchi in the healthy lung contain only a small quantity of frothy mucus ; they are patent. The mucous surface is as a rule somewhat wrinkled longitudinally.

The lung may be compared to a bunch of grapes, the stalks being the bronchi and the grapes the air vesicles. These bronchi divide regularly and dichotomously, but the division of the two largest bronchi takes place in a different manner in the two lungs. On the left side it runs for some distance before dividing, and then one

branch goes to the upper lobe of the lung and the other to the lower lobe, whilst on the right side the bronchus divides almost immediately into two branches, the lower of which goes to the lower lobe of the lung, whilst the upper one soon subdivides, the lower branch going to the middle lobe and the upper branch to the upper lobe. These bronchi divide and subdivide until they come down to the smallest or terminal bronchi, one of these terminal bronchi having around it a system of bronchioles and air vesicles, which together form what is known as a lobule. On examining the pleural surface of the lung, it is found that this division into lobes and lobules is not at all an artificial one, the lobes being readily enough discerned as a series of polygonal areas, each area being surrounded by a kind of network of black lines. Each of these polygonal areas is spoken of as a lobule, and the air vesicles which form this lobule all communicate with a terminal bronchus. On making a section perpendicular to the pleural surface, it will be noted that the black lines run into the substance of the lung for some distance, and in many cases appear to be intimately connected with a similar tissue which surrounds the bronchi. Accompanying the bronchi, at the root of the lung, and passing into the organ along with them, is a mass of connective tissue, which supports a series of structures to which reference will afterwards be made. The black lines already examined on the surface of the lung will be found later to be bands of connective tissue (interlobular septa), from which finer septa are sent out between the smaller groups of air vesicles. These form a strong supporting network of connective tissue, the large bands of which are situated at the entrance of the bronchus on the one hand, and on the other they form a strong covering to the lung, from which bands of considerable size run into the substance of the organ, to meet the masses of connective tissue prolonged along and from the bronchi.

This connective tissue framework, as in other organs, supports not only the characteristic structure of the lung, but also serves as a medium in which the blood-vessels, nerves, and lymphatic vessels and spaces may ramify before they come into direct relation to the alveoli.

In order to understand the openings in the tissue which may be seen in any specimen of normal lung under a low power, it will be

well to describe the structure of one of these lobules, as the structure has a very important bearing on the relation of the cavities in certain diseases, such as emphysema and phthisis. When the terminal bronchi, or the last branches resulting from the dichotomous division of the bronchi are reached, it is to be noted that numerous small branches, more or less at right angles to the terminal bronchi, or continuous with it at its termination, are given off. These vary in number somewhat, but there appear to be at least six of them. Each of these divides into two branches, spoken of as the terminal bronchioles. At the end of the terminal bronchiole is a tuft of two or three small tubes, each of which continues as such for a short distance, and then suddenly opens out into what is known as an alveolar passage. The walls of this alveolar passage are delicate, and are

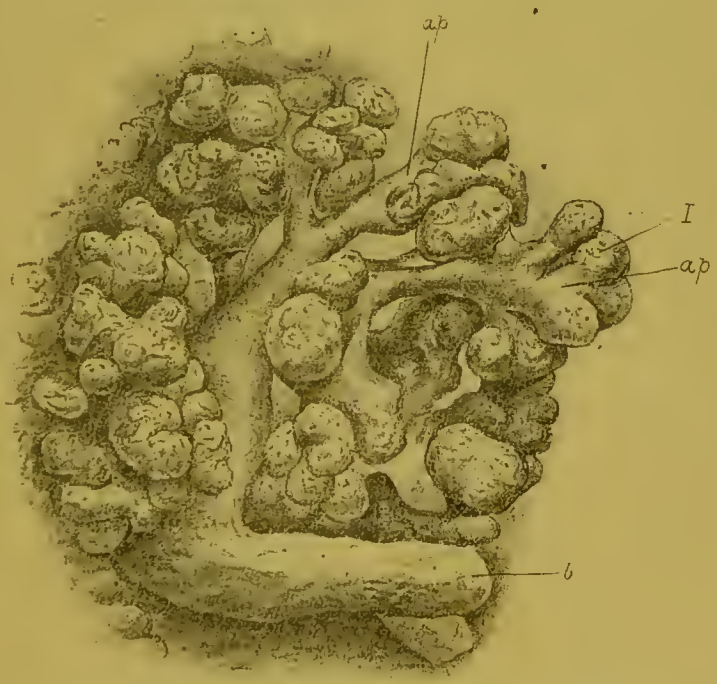


FIG. 57.—Drawing from fusible metal cast of the air cavities of a fœtal lung, made and kindly lent by C. W. Cathcart. (× 30.)

b. Terminal bronchus, from which lateral branches are given off at right angles.

a.p. a.p. Alveolar passages, opening into which are the infundibula (*I*).

On the surface of some of the casts of the infundibula the markings corresponding to the septa of the air vesicles may be seen.

throughout their whole extent formed of air vesicles, which have a somewhat different arrangement at different points. Along each side of

the passage are larger pouches, which in their turn are lined by air vesicles, and between the openings of the pouches there are simply air vesicles surrounding the alveolar passage, and these air vesicles are continued from this point around the walls of the larger pouches, as above. At the end of the alveolar passage, similar large pouches are met with, lined in the same way by the air vesicles. The pouches at the sides are spoken of as the lateral infundibula, whilst those at the end are spoken of as the terminal infundibula. The alveolar passages in connection with a terminal bronchiole, with their infundibula and air vesicles, make up a lobulet or acinus, whilst the whole of the acini in connection with a terminal bronchus go to make up a single lobule, the base of which is seen on the surface of the lung as the polygonal area surrounded by the dark pigmented connective tissue. Supporting these various cavities is the connective tissue, first of all between the various lobules, as the interlobular septa; then as prolongations running towards the centre of the lobule, and from the centre towards the periphery from the connective tissue surrounding the bronchus. These together form a network of connective tissue supporting the various cavities, a basis in which the lymphatics and lymph spaces may run, and a support for the blood-vessels and nerves which run around the terminal air cavities.

With the larger bronchi in the peribronchial tissue run both pulmonary artery and vein, as well as the bronchial vessels, which are much smaller in size (see Fig. 58); but with the smaller bronchi it is to be noted that only the pulmonary artery runs along with the bronchus, the pulmonary vein being situated at the periphery of the lobule, so that on making a section through a larger bronchus and its accompanying vessels three openings of considerable size are seen; whilst on making a section through one of the terminal bronchi only two openings are seen together—the bronchus and the pulmonary artery; whilst the third opening—the pulmonary vein—is situated some little distance away.

In a section of healthy lung prepared in Müller's fluid (§ 53, p. 42), or chromic acid (§ 57, p. 44), stained in picro-carmine, under the low power (× 50), note first the pleura, the interlobular septa, then the bronchi with their accompanying vessels, and lastly, the air chambers, into which these bronchi open.

The pleura is seen at one margin of the section (the smooth surface). Under the high power (× 300) it is at once seen to be divided into two distinct layers, over which again, in very carefully made pre-

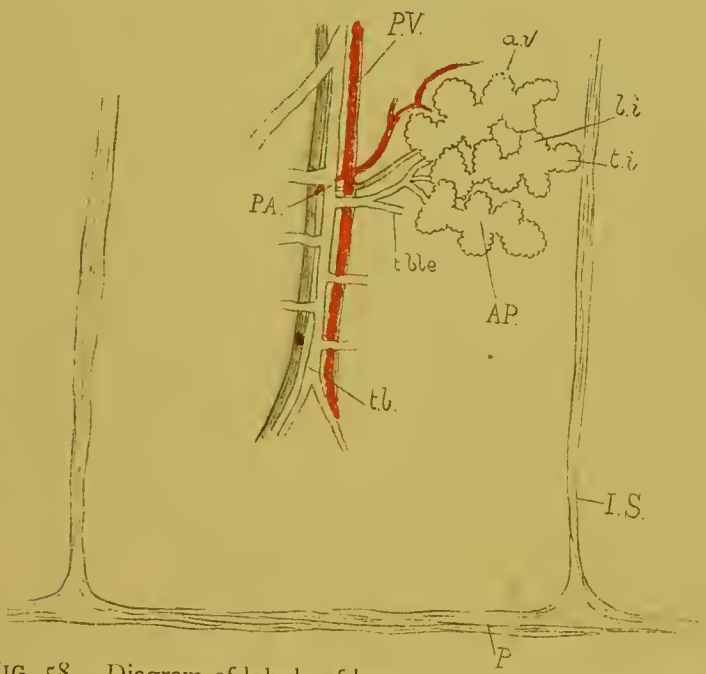


FIG. 58.—Diagram of lobule of lung.

t.b. Terminal bronchus.
t.ble. Terminal bronchiole, from which open the small alveolar ducts.
A.P. Alveolar passage.
l.i. Lateral infundibulum.
t.i. Terminal infundibulum.
a.v. Air vesicles.
P.A. Branch of pulmonary artery.
P.V. Branch of pulmonary vein.
I.S. Interlobular septum.
P. Pleura.

The three alveolar passages constitute an acinus, the parts between the interlobular septa a lobule.

parations, may be seen a layer of endothelial cells—large flattened nucleated cells—which, seen in a section taken from a fully expanded lung, are spindle-shaped. The outer layer of the pleura, immediately below this layer of cells, is made up of fibrous (pink) and elastic (yellow) tissue in bundles. In this are seen a number of blood-vessels, whilst between the bundles are numerous small plasma spaces or lymphatics. Between these lymphatics and those of the next layer there is not a free communication, but the superficial lymphatics communicate freely with the pleural cavity.

Beneath this is the deeper, more areolar looking layer, or subpleural tissue, which is considerably thicker than the superficial layer, but which, like it, is made up of fibrous tissue, with connective tissue cells and bands of yellow elastic tissue. It is freely supplied with blood-vessels, some of them of considerable size (filled with greenish corpuscles—greenish because of the staining with picric acid). The lymphatics in this layer can usually be readily distinguished, as they are found to contain small quantities of pigment, even in the healthy lung.

Continuous with this more open layer are the interlobular septa, the structure of which is very similar to that of the subpleural layer. These septa are seen to send off small branches, to support the parenchyma of the lung; but the septa themselves are prolonged to meet the connective tissue surrounding the bronchi, so that several bands of fibrous or connective tissue are seen in direct continuity between the subpleural layer and the walls of one of the bronchi. In all these there are numerous lymphatic vessels and spaces.

The structure of the bronchi.—Under a high power (× 300).—First, lining the tube, is a layer of *ciliated* epithelium, the cells of which are distinctly columnar in the larger bronchi, but are shorter, though still retaining their cilia, in the smaller bronchi. Some few of these are seen as goblet cells lying between the ciliated cells. Between these, and at a lower level, are a number of ovoid cells, which appear to be imperfectly developed ciliated cells, whilst still deeper is a layer of flattened cells or Debove's layer. These cells rest on a delicate homogeneous layer or basement membrane (which stains pink), found only in the bronchus of man (Hamilton). This appears to play a very important part in bronchitis and bronchiectasis. It is very elastic, may be stretched to an enormous extent, and is not easily affected by reagents.

Beneath this is a fibrous coat, in which are nuclei of connective tissue and a number of white blood corpuscles, whilst running through the tissue are some yellow elastic fibres. Then comes the muscular coat, made up of circular bands of non-striped muscular fibres, in which the rod-shaped nuclei may be readily distinguished. It is to the contraction of these fibres that the longitudinal folds described under naked eye appearances are due. Then external to this comes the

outer fibrous or connective tissue coat, in which are the bronchial cartilages, the mucous glands extending inwards between the cartilages, and the bronchial artery and vein, sections of which are seen, and continuous with this outer fibrous coat are the interlobular septa. Around the smaller bronchi in this coat the quantity of yellow elastic tissue is considerable, whilst the glands and cartilages gradually diminish in number.

To examine the terminal air cavities, it will be necessary to take a silvered preparation, say of the lung of a cat. Low power (× 50).—Note the air cavities. Some of them are seen as small polygonal openings, bounded by a more or less tortuous line. On each side of this line may be observed a network of tortuous lines, resting on which are a few small round nuclei; others with similar boundaries are considerably larger, and instead of being polygonal in shape, appear almost like the section of part of a racemose gland; others again are more or less rounded or oval, with a series of indentations along their walls. These correspond to sections through alveolar systems, infundibula, &c., and the student should make a careful study of these various openings, in order to be able to recognise the parts of which they are sections.

On examining this section under a high power (× 300), the investigator sees that the irregular lines are blood-vessels running at the margins of the air vesicles, or in the angles between the septa. The network of capillaries forms the floor of the air vesicle, between the meshes of which are seen delicate bands of elastic fibre. Separating the blood-vessels from the air are epithelial cells, of which there are two kinds: more or less cubical cells, which are situated chiefly in the alveolar duct, and at the angles between adjacent infundibula and adjacent air vesicles, and also a few in groups at intervals on the floor of the air vesicles; and, between these, large flattened cells, each of which has a rounded nucleus, and the outline of each is marked out distinctly by the cement substance stained brown by the nitrate of silver. At intervals along these lines are clear spaces—the so-called stomata—which are apparently due to the heaping-up of cement substance at these points.

A complete air vesicle, then, is a cup-shaped cavity lined with epithelium, either flattened or cubical, which rests on a fine network

of capillary vessels. Supporting the capillaries is a delicate connective tissue. These cups placed side by side form the walls of the pouches or infundibula, which are given off from the alveolar passages, and they also make up the walls of the alveolar passages in the intervals between the infundibula. In the angles between these cups are larger vessels; the walls of the cups cut transversely appear as the outlines of the air vesicles. (See Fig. 58.)

Acute Pneumonia.

179. Synonyms.—"Common," "Lobar" (from the fact that, as a rule, the whole of one or more lobes becomes affected in this condition), "Sthenic" (from the type of the symptoms), "Fibrinous," "Exudative," or "Croupous" (because the nature of the exudation appears to be similar to that which forms the false membrane in croup,—"Croupous" is not an appropriate name); and lastly, "Pleuro-Pneumonia" (as this form of pneumonia is almost invariably accompanied by pleurisy, with an exudation of fibrinous lymph on the pleural surface).

The process may be divided into four stages, and of these it will be necessary to examine sections from the first three. The four stages are—

1st. Stage of congestion or engorgement, during which there are (*a.*) hyperæmia, (*b.*), effusion.

2d. Stage of red hepatization.

3d. Stage of grey hepatization.

4th. Stage of resolution.

It is in very rare cases only that the lung is examined in the early stages of this disease. The changes which occur in the first stage are characterised by the following appearances.

Stage of Congestion.

180. In this condition there is apparent to the naked eye, at the base and posterior margins of the lung, a marked congestion of the vessels on the surface of the pleura; under the pleura small hæmorrhages are seen, and the substance of the lung is somewhat firmer than it is towards the apices, but it is not solidified. It is rather more friable than the normal lung tissue. On making a section it

will be observed that the surface is of a bright arterial red colour, and somewhat œdematous, owing to a retardation of blood flow, in consequence of which the blood is longer in contact with the air, which is still freely entering the lungs before death. On squeezing a portion of the tissue a bright red or watery fluid mixed with air is forced out; this fluid, examined under the microscope, is found to contain a considerable number of red blood corpuscles, but these appear to come from the blood-vessels. A piece of this portion of the lung thrown into water does not sink, as it is buoyed up by the air, which, as already seen, freely enters the air vesicles.

Harden in chromic acid (§ 57, p. 44), or in Müller's fluid (§ 53, p. 42), stain a section in picro-carmine (§ 73, p. 53), and mount in Farrant's solution (§ 98, p. 71).

Under the low power (× 50) a peculiar beaded appearance of the vessels bounding the air vesicles is observed. The capillary network is also distinctly marked out, whilst in the space bounded by these

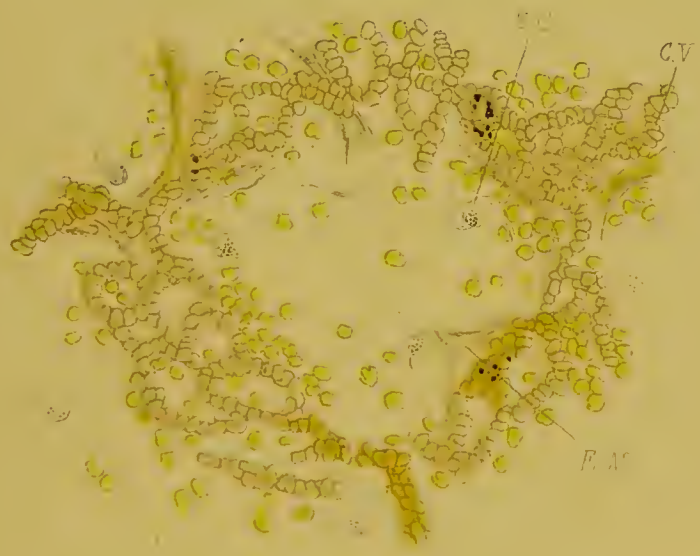


FIG. 59.—Drawing of section of congested lung, stained with picro-carmine. (× 300.)

C.V. Distended capillary vessels of vascular network in the wall of the air vesicle.
E.C. Detached epithelial cells.
E.M. Elastic membrane, forming part of the wall of the air vesicle.

vessels a number of small pink nuclei may be discerned, and similar nuclei may be seen studding these beaded vessels.

High power (× 300).—The capillary vessels are now seen to be considerably distended, and are naturally injected with closely packed greenish cells, which are recognised as blood corpuscles. Where portions of the capillary network are to be seen they also are filled with these greenish cells, whilst a few may have escaped into the air cavity, where they may be recognised by their double outline and pale green colour. The epithelial cells are swollen at some points, whilst at others they are undergoing proliferation, or some of the large flattened cells are separated directly from the capillaries, and are seen lying free in the alveolar cavity. Only here and there throughout the whole section is there any further effusion into the air vesicle; but when there is any such further effusion its characters are similar to those presented during the stage of red hepatization. The effusion may be in the form of slight hæmorrhages from ruptured capillaries. There comes a point, however, at which the effusion into the air vesicles becomes a very marked feature; and as soon as this is reached, and the material has coagulated, the stage of true red hepatization of croupous pneumonia is reached.

Stage of Red Hepatization.

181. *Naked eye appearances of the lung in this condition.*—The lung, or a lobe of the lung, has now become a solid mass, as all the air vesicles are filled with a coagulated fibrinous effusion. As a rule, it is found that this solidification is confined to one of the lobes—the lower one—and in this the condition is most marked at the posterior part. This arises from the fact that at first the effusion is fluid, and hence gravitates to the most dependent parts, where it afterwards consolidates. It is sharply marked off from the rest of the lung tissue, in which there is, as a rule, marked congestion and œdema. In certain cases the whole of the organ may be hepatized; in which event the lung, instead of weighing about one pound, may weigh two, three, or even more, from the large amount of exudation into the air cavities. On examining the pleura it will be observed that there is frequently considerable injection of its superficial vessels, or there may be a layer of fibrinous lymph thrown out on the serous surface; in the later stages of the disease, the

presence of this evidence of pleurisy may invariably be determined. On making a section into the affected lobe the knife meets a tough, somewhat resistant and elastic tissue; but as the tissue is quite solid, it "cuts" readily, and does not give way before the knife. The cut section has a dull, or, after a time, a bright red, smooth, glistening appearance, mottled with paler and grey spots, though this glistening may in some cases give way to a slightly granular appearance, especially in the later stages of the red hepatization. The tissue is evidently quite solid (as it sinks in water), and the surface is often compared to a section of red granite. When handled, the substance feels somewhat firm, almost like a piece of leather, but it is friable, and the fingers may be made to meet in the tissue considerably more readily than in a normal lung. On squeezing, only a very small quantity of bloody serum exudes from the cut surface. The mucous membrane of the bronchi is injected, and the bronchi frequently contain a bloody, frothy, or viscid fluid. In the smaller bronchi small firm casts may be found, similar to those met with in the air vesicles. Stain a section in picro-carmine (§ 73, p. 53), and examine under a low power (× 50). Observe that the air cavities, in place of being empty, are *filled* with a delicate-looking film, through which *light is readily transmitted.* Here and there throughout the film are seen nuclei. The blood-vessels forming the outlines of the air vesicles are less distinctly seen than in the normal lung, and sometimes contain much less blood.

Examine a piece of the pleura, and note that the vessels in its deep layer and in the interlobular septa are engorged with blood, that there is considerable thickening of the fibrous tissue in these layers, and that on the surface of the pleura, often above the flat cell layer, is a quantity of material which has all the characteristics of that seen filling the air cavities and the smaller bronchi, except that it is stained somewhat more brown, is more granular looking, and is not quite so transparent.

High power (× 300).—First examine the exudation in the air cavities, which is seen to be composed of a delicate network of coagulated fibrin, filaments of the network being attached to the walls of the space, so that the coagulum completely fills and even distends it; entangled in this mesh-work of fibrin are a number of

coloured blood corpuscles, recognised by their double outline and greenish colour. In addition to these, numerous colourless

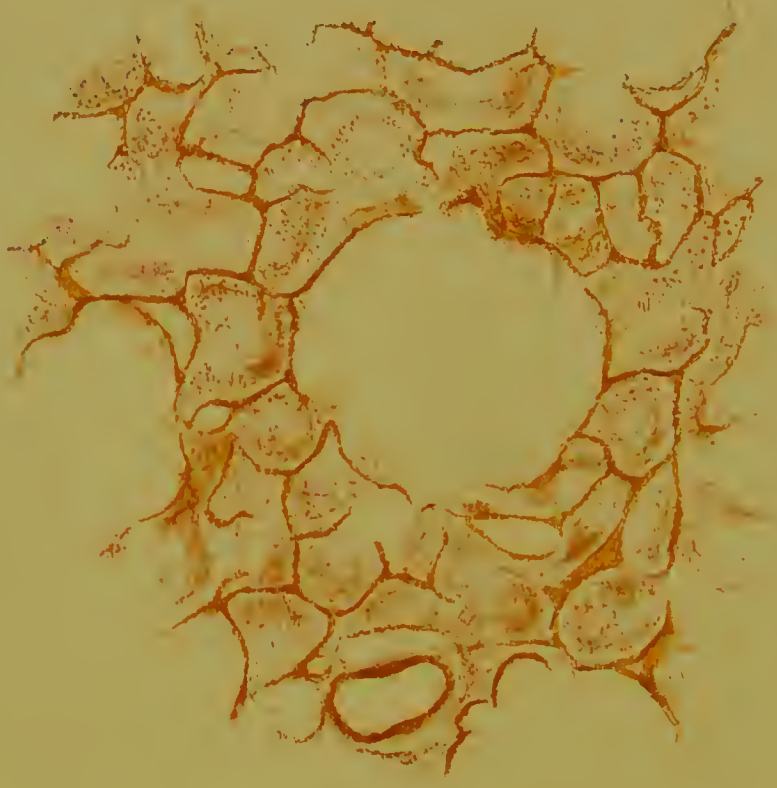


FIG. 60.—Drawing of section of lung in a condition of acute pneumonia, stage of red hepatization, stained with picro-carmine. (× 50.)

In the centre is seen a larger air passage, not filled with the coagulum.

In the smaller air cavities the delicate strands of fibrinous lymph and the cellular elements of which the coagula are composed are seen. The capillary blood-vessels are readily distinguished. Note the transparency of the clot, and that it does not take on the staining material at all readily. Observe also that the clot completely fills the air vesicle.

blood corpuscles, stained pink, are seen. These appear in some cases to be nucleated, and to be somewhat larger than the coloured blood corpuscles. At certain points larger groups of these blood corpuscles are found; these have been poured out through a rupture in the wall of the vessel. The more scattered corpuscles have come through the walls of the vessels during the process of diapedesis, and have been entangled in the coagulum formed from the exuded blood elements.

In this clot still another form of corpuscle is met with—large nucleated cells, which will be at once recognised as similar to those



FIG. 61.—Drawing of air vesicle with contained fibrinous exudation. Red hepatization, stained with picro-carmine. (× 300.)

c.v. Blood-vessels in interalveolar septa, in this case somewhat distended with blood.

f. Filaments of fibrinous lymph attached to the wall of the air vesicle, and not deeply stained.

E.C. Large nucleated epithelial cell.

The white and red blood corpuscles may also be seen entangled in the meshes of the fibrinous network, the white stained pink, and the red green, with a double outline.

lining the air vesicles. They are derived from the swollen and proliferating epithelial cells, or some of the more flattened plates are simply separated during the first stage of the process and are entangled in the fibrinous network. It is found thus far that the majority of these cells are near the wall of the air vesicle, though a solitary one may be met with here and there throughout the network. Now examine the blood-vessel in the wall, and it will at once be seen that around it is an exudation of leucocytes into the delicate connective tissue which accompanies the capillary vessel, and there is probably, at the same time, a proliferation of the connective tissue corpuscles, so that here the first indication of an interstitial process

is met with, which in some pneumonias may become a very prominent feature. There is no difference in appearance between the leucocytes and the connective tissue corpuscles, both of which are seen in the early stage as small rounded carmine-stained bodies. The exudation on the pleural surface is found to be made up of similar elements—coagulated fibrin, red and white blood corpuscles, with, in some cases, a few flattened cells derived from the endothelial layer which covers the pleura.

Stage of Grey Hepatization.

182. *Naked eye characteristics.*—The lung here also is considerably heavier than normal. The exudation is found in the same positions as the red hepatization, of which this is a later stage. Here, too, the affected part of the lung is solid, but does not appear engorged; frequently the lobe above that in which there is grey hepatization is in the red stage or is deeply congested. On the surface of the pleura a layer of coagulated lymph is invariably met with. The tissue is heavy, firm, solid, and sinks in water, "cuts" readily, and is extremely friable, so that it breaks down very easily under pressure between the finger and thumb. The red colour has given way to a yellow or reddish grey, and the tissue has been compared to grey granite in appearance. The cut surface has a finely granular appearance, very characteristic of this condition. The bronchi in this stage of the disease, if not in the red stage, are generally somewhat congested. On scraping the surface of a section of the lung and examining the scraping under the microscope, the yellowish particles which come away along with muco-purulent material are seen to consist of small casts of the air cavities, alveolar passages, infundibula, or even of the small terminal bronchioles. On adding acetic acid to the masses mixed with water, there is a precipitation of mucin; and if some of the casts be treated with osmic acid (one-sixth per cent. solution) for a few hours, teased out and exposed to the light, and mounted in Farrant's solution, they are stained black; whilst with picro-carmine or logwood they are also stained deeply. Harden in Müller's fluid (§ 53, p. 43), or chromic acid (§ 57, p. 44), stain a section in picro-carmine (§ 73, p. 53).

Examine under a low power (× 50). The air vesicles contain a deeply stained granular-looking material, which does not completely fill the cavity. Between this material and the vessel in the wall is a distinct interval. The vessels apparently contain but little blood. They are, nevertheless, distinctly seen. The pleura is thickened as in the stage of red hepatization, and around the engorged blood-vessels of the interlobular septa and the pleura a considerable number of deeply stained small round cells are seen. On the pleural surface is a mass of coagulated fibrin, which under this power is opaque, granular looking, and deeply stained.

High power (× 300).—A mass of brownish-pink cells may be observed. The fibrin filaments have broken down and become granular, and the red blood corpuscles have disappeared. The white blood corpuscles, or leucocytes, have become much more abundant, and are evidently undergoing degenerative changes, for they now appear to contain three or four nuclei, and are thus like pus corpuscles. The whole mass appears more or less granular, and obstructs the passage of light, whilst as under the low power it appears of a brownish-pink colour, and is separated from the wall of the air vesicle by a distinct interval. Now examine the wall in which the vessel is somewhat compressed, and contains but little blood. Here are seen more of the rounded cells, stained pink, lying around the vessel, with here and there a young connective tissue cell becoming slightly elongated or spindle-shaped. Young epithelial cells may also be seen on the wall of the cavity. Around the vessels in the interlobular septa and in the pleura are small round cells, whilst on the surface, in the deeply stained, opaque, granular looking lymph, loops of blood-vessels are frequently to be distinguished passing from the vessels of the pleura. The vessels in the peribronchial tissue are engorged, and surrounded by a number of leucocytes and young connective tissue corpuscles.

Stain a second specimen in osmic acid (one-sixth per cent.) for twenty-four hours, examine (× 300), when it will be observed that all the leucocytes are more or less fatty, and that between them are fatty granules and globules all stained black, whilst in certain cases the lymphatics around the air vesicles are marked out by the black stained fatty particles lying in them.

Stage of Resolution.

183. If a specimen is examined during the stage of resolution, the tissues are still pale, but they are becoming softer and more flabby to the touch, a considerable quantity of a soft muco-purulent material may be squeezed out, along with which are the smaller fatty casts of the air vesicles. Harden in chromic acid or Müller's fluid. Stain a section in osmic acid (§ 80, p. 62), and mount in Farrant's solution (§ 98, p. 71).

Low power (× 50).—The mass in the air vesicle is now much further removed from the walls, and is deeply stained, and the black particles and globules are especially numerous. The whole section appears to be granular, and the blood-vessels are more prominent.

High power (× 300).—The material in the air vesicles is made up of fatty granules and globules, some of which are evidently taken into the lymphatics around these air vesicles. In the blood-vessels the red blood corpuscles may be seen in considerable numbers. Then, too, it is to be noted that epithelial cells are to be found covering the capillary network, these cells taking the place of those which were shed. They appear to be derived from the small cubical cells which have been described as present in groups, especially at the angles between adjacent air vesicles. The walls of the air vesicles are much more prominent during this stage of the disease, owing to the distended lymphatics, the return of the blood to the capillary vessels and the new formation of epithelium.

Other terminations of pneumonia may be—(*a*) death during one of the earlier stages of the disease; (*b*) abscess formation, where the inflammatory condition is very acute; or (*c*) gangrene may occur where the blood supply is rapidly and completely cut off by the great amount of effusion into the air cavities. In this condition there is the characteristic sloughy appearance, and an intensely fœtid odour. This will be very readily recognised, and it is beyond our province, in a practical work devoted to the consideration of the more common forms of diseased tissues, to enter into any detailed description of the various processes.

Pleurisy.

(*For description of Pleura, see* § 178, *p.* 227.)

184. Pleurisy may be divided into three stages :—

1*st*. Stage of congestion.

2*d*. Stage during which there is an effusion of lymph from the congested vessels on to the pleural surface, accompanied by an effusion of serous fluid.

3*d*. Organisation in lymph, with absorption of fluid, or softening and partial absorption or suppuration of the exuded products. Four stages are usually described, but for descriptive purposes the above classification answers very well.

The naked eye appearances differ considerably in these three stages, but the microscopic changes follow one another in regular course. Of these stages examine sections in the second and third only.

In the first stage of a simple pleurisy the vessels of the superficial layer of the pleura are distended with blood, and are seen tolerably distinctly through the layer of endothelial cells.

During the second stage the pleura becomes cloudy and granular looking, the surface is dry, and on careful examination a thin layer of soft lymph, which can be scraped off as a delicate film with the finger nail, may be observed covering the congested surface. Harden a piece of the lung with the attached pleura in chromic acid (§ 57, p. 44), or Müller's fluid (§ 53, p. 42). Stain a section in picro-carmine (§ 73, p. 53).

Low power (× 50).—If the pleurisy be simple, the changes take place principally in the superficial or dense layer of the pleura. There appears to be distension of the blood-vessels, and even at this stage exuded leucocytes are seen as bright pink specks around the turgid blood-vessels. On the surface of the lung a delicate, almost transparent, layer of fibrin may be seen, with a few small pink nuclei scattered through its substance.

High power (× 300).—The dots around the vessels are pink-stained leucocytes or wandering cells, though a few of them are probably

proliferating connective tissue corpuscles, even at this early stage. The transparent layer on the surface resembles very closely the material that was found in the alveoli in red hepatization, the delicate filaments of fibrin running in all directions forming a network, in the meshes of which are entangled coloured and colourless blood corpuscles, sometimes in considerable numbers. This film of lymph is most frequently thrown out on the endothelial surface, so that beneath the delicate coagulum the somewhat swollen endothelial cells may be seen in profile as spindle-shaped cells with pink-stained nuclei. Sometimes, however, these cells are detached by the exudation, and are consequently found entangled in the fibrinous lymph.

This is all that is to be seen in the case of a simple pleurisy, but pleurisy is, as has been noted, an almost constant accompaniment of pneumonia. In such a case it is found that the vessels of the deep layer are congested, and that numerous leucocytes are collected around them, along with which there also occurs some slight swelling of the bands of fibrous and elastic tissue, so that, apart from the exudation of lymph, there is some thickening or swelling of the pleura proper. Later in this stage, during which the effusion of fluid takes place into the pleural cavity, there is on the pleural surface a thick soft elastic layer which when taken from the pleural cavity presents a more or less honeycombed appearance, if the quantity of fluid be small. Sanders used to liken this to the appearance obtained when two slices of bread and butter were pressed together and then separated; but if the fluid is present in considerable quantities the surface is smooth. This layer of lymph may be stripped off as a soft, easily broken membrane, leaving the pleural surface perfectly smooth. A section hardened, stained, and examined as before is found to present much the same appearances as the last specimen, except that the fibrinous layer is considerably thicker and more granular. It contains a greater number of leucocytes, and stains somewhat more deeply, often of a peculiar brick red tinge, but it still retains some of its transparency. Around the vessels the number of exuded and proliferated corpuscles is considerably increased. During this stage the lymphatics appear to be choked up by the fibrinous lymph, and, in a well stained section, they may even be seen filled with the granular looking material.

In what may be described as the fourth stage, the lymph has formed a matrix in which organisation may take place, though there is no organisation of the lymph itself. The lung in this condition is more or less firmly adherent to the wall of the chest, as the two inflamed surfaces have come together; a temporary adhesion has been brought about by the sticking together of the two surfaces of soft lymph after the absorption of the fluid part of the exudation. This may be readily broken down, but it is impossible to detach the whole of the lymph from the pleural surface, and at the points from which it may be detached the surface is left rough and irregular, and evidently something more than the pleura is left. Harden a portion of such a lung in Müller's fluid (§ 53, p. 42), or chromic acid (§ 57, p. 44), stain in picro-carmine (§ 73, p. 53), and mount in Farrant's solution (§ 98, p. 71).

Examine a section (× 50). The section under consideration was taken from a case in which there had been pleurisy of some standing, and where there had been several exacerbations of the disease; the pleura was extremely thickened, whilst on the surface was a layer of soft lymph, as described above; there is evidence of considerable congestion of the interalveolar capillaries. The vessels in the wall of the bronchus and in the interlobular septa are also filled with blood.

Around these vessels considerable numbers of stained nuclei are readily distinguishable. Passing outwards to the pleural layer, it is seen to be considerably thickened, and the distinction into two separate layers is altogether lost; its deeper part appears to be made up of swollen fibrous tissue, between which the blood-vessels are numerous, and are filled with coloured blood corpuscles, whilst the superficial part of this layer is composed of a more delicate nucleated reticular tissue, in which may be seen large sinuses, and lining the walls of these are a few coloured blood corpuscles, seen as a thin green line; there are also numerous smaller vessels, which appear as loops or branching lines, all of them having their long axes more or less perpendicular to the surface. At certain points these vessels appear to have given way, for several masses of green corpuscles are seen at the point where this cavernous tissue ends. Above this is a layer of dense looking tissue stained pink, into which vascular

loops, recognised as green lines, may be seen running more or less obliquely to the surface. Even in this layer there may be seen a few small brick red masses, which are to be recognised as remnants of fibrin. The next layer, which is almost entirely composed of fibrin, is very granular looking. It takes on the picro-carmine staining as a deep brick red colour, whilst very little light is allowed to make its way through. Greenish looking streaks may be observed in this, usually as Y-shaped lines, or in the form of more or less perfect loops. Around or near these greenish rods are seen small green patches, irregular in size and shape, which will at once be recognised as small hæmorrhages. These hæmorrhages are especially numerous towards the surface of the deeply-stained layer of lymph. This and the preceding layer are in reality of the same age, but the process of organisation and absorption of lymph is evidently much further advanced in the deeper part of the layer, or that part into which the vascular loops first make their way. Above this layer again is a delicate translucent layer of newly effused lymph, which has coagulated in the form of delicate fibrils, entangling coloured and colourless corpuscles in the meshes. This layer is not deeply stained.

Each of these layers as described shows exceedingly well the process of organisation going on in the fibrinous clot, and at each level the organisation is at a definite stage, in which the processes of that period may be readily observed. It must be remembered that in sections taken from lymph undergoing organisation on an inflamed pleural surface only one or two of these processes can, as a rule, be made out, but in the specimen described there is an example of several of them combined.

High power (× 300).—The congestion of the vessels surrounding the air vesicles in the interlobular septa in the peribronchial tissue and in the layers of the pleura is now more readily discerned. All the vessels in these situations are evidently distended, and packed with the small greenish corpuscles with double outlines. Around these various vessels the exuded leucocytes and young connective tissue corpuscles are seen in large numbers as pink bodies; and if these are more carefully examined, say in one of the interlobular septa, some of them are seen to be rounded, others are oval, and others again are becoming more or less spindle-shaped.

Now examine the more open part of the pleural layer, or that part in which, under the low power, the large open sinuses were seen. Here there is evidently a considerable quantity of new connective tissue, and the original pleural layer can be distinguished only by the presence of pigment in the lymphatics of the deeper part of this layer. Above this is a delicate, clear, wavy line dividing the deep from the superficial layer of the pleura, the latter of which has evidently merged into the new or organised tissue. This is made up of numerous branching or spindle-shaped cells, each with a distinct nucleus. Between these cells is a variable quantity of a fibrillated stroma. In this layer are to be noted vascular openings, varying considerably as to the thickness of the wall and the size of the lumen. Towards the deeper part are vessels with relatively thick, well organised walls, in some of which can be discerned a distinct muscular coat, and an endothelial lining. These appear to be the pre-existing vessels of the pleura, which in some instances are considerably dilated, and are almost invariably filled with coloured corpuscles (stained green). Throughout the whole of this layer, but more especially towards the surface of it, are numerous large rounded or oblong openings, the walls of which are formed of one or several layers of compressed or flattened connective tissue corpuscles, seen as nucleated spindle-shaped cells. Within the thin walls of some of these spaces are a few coloured blood corpuscles, but the greater part of this large vascular channel is empty in most cases in the section under consideration.

Lastly, observe a number of small capillary channels in the connective tissue. These small vessels are of the very simplest structure. They may be distinguished as bounded on each side by a single row of elongated spindle-shaped cells, and they may be seen running in various directions; but the majority of them run at right angles to the surface, though from the number of transverse branches it is evident that these capillaries are really in the form of loops, with the convexity of the loop towards the surface. Between the double row of cells a single row of coloured blood corpuscles is discernible. These capillary loops (Fig. 62) are in structure very much like the vessels running in the substance of a sarcoma, and as in that tumour, so here, the blood has made its way from the capillary into the surrounding tissue, in some cases the delicate vascular wall having

yielded to very slight sudden increase of blood pressure. In this specimen small extravasations have occurred at the superficial sur-

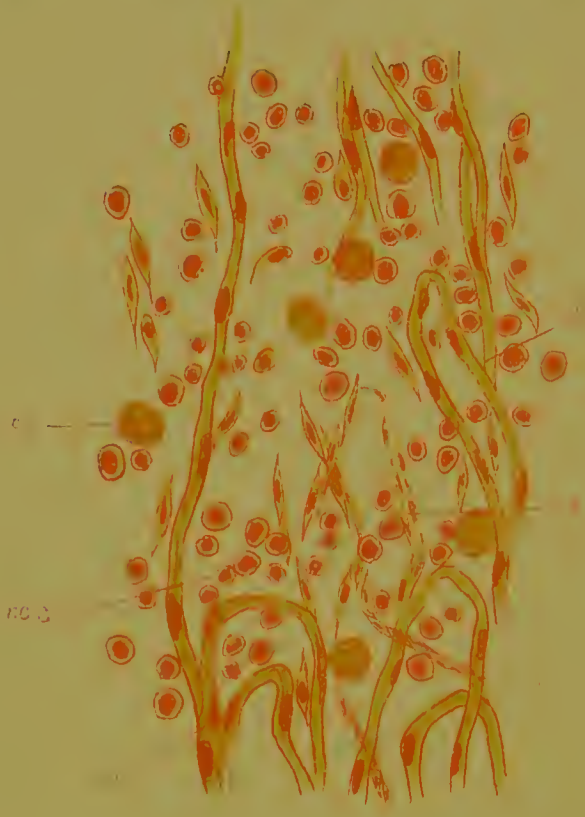


FIG. 62.—Loops of blood-vessels in organising tissue on a serous surface. Section stained with picro-carmine. (× 300.)

v.l. Loops of vessels fully formed, the structure of which is very readily observed.

c.s. Double rows of spindle-shaped connective tissue cells, from which the embryonic vessels are formed. Most of these cells are arranged with their long axes at right angles to the surface.

c.l. Large cells met with in all granulation tissue derived from connective tissue cells.

n.c.s. Small round cells or leucocytes.

face of this layer. Above these extravasations is the more solid looking pink layer (seen under the low power).

Passing from below upwards, the following structures may be observed in this pink layer. At the deeper part are numerous spindle-shaped connective tissue cells, which may be arranged into two groups, one set passing at right angles to the surface, arranged principally in double rows. These rows are frequently separated by lines of green discs, or coloured blood corpuscles, so that these may be looked upon as the cells of which the walls of the new blood-

vessels running at right angles to surface are built up. The cells of the second set are placed with their long axes more or less parallel with the surface; they are spindle-shaped also, and have lying between them a clear pink, homogeneous material, which as a rule presents but little trace of fibrillation. In the deeper part of this layer there is little or none of the granular degenerating lymph which forms such a decided feature of the upper part of this same layer. This lymph first makes its appearance as thin flattened masses of brick red colour, between which a tissue similar to that already described as present in this layer is found. It will be noted that the homogeneous material lying between the cells is not stained a very deep pink, and it appears to be present in smaller quantity. The newly formed vessels, too, run in between these masses of lymph in all directions, some of them at right angles to, others obliquely to or parallel with, the surface. Passing outwards, the lymph becomes more noticeable, and is now seen as the large brick red granular masses, in which are a few vessels surrounded by a number of more or less rounded cells. In this part of the lymph the organisation is at its very earliest stage. The walls of the vessels are of purely embryonic type, and are formed of cells—some of them a little flattened—laid end to end, and between these the blood may be seen forcing its way. In some parts of the section it is difficult to distinguish any wall to the vessel; the blood corpuscles appear to be simply pushing their way into the fibrin. In spite of this some of the sections of vessels are of considerable size. Here the connective tissue cells are not only young, but they are scarce. At the point where the layer of granular lymph stops, there are numerous small extravasations of blood, the blood having escaped from the ruptured young vessels during the last process of inflammation, when the last layer of lymph was exuded. This most recent layer of lymph is seen lying superficial to the greenish corpuscles of the extravasated blood. It is made up of a network of fibrin similar to that described as present in the air vesicles during the stage of red hepatization in acute pneumonia. Entangled in this network are a few white blood corpuscles, not nearly so many as are found in the air vesicles; there are also numerous red blood corpuscles. This layer has already been described as occurring in a recent pleurisy, so that it has been exuded

some considerable time after the layer immediately beneath it, and a still longer time after the layer which was in contact with the superficial layer of the pleura.

Bronchial Catarrh, or Acute Bronchitis.

185. This is most frequently met with in cases of measles, whooping-cough, &c. As an uncomplicated disease, acute bronchitis seldom comes into the hands of the pathologist. In such a condition the lung is congested, and on exposure to the air for a few minutes the section assumes a bright red colour. In the bronchi there is a "yellow muco-purulent fluid which covers the surface of the mucous membrane, and can be pressed out in the form of a tough tenacious pellet." The adventitia of the bronchus is greyish white, whilst the mucous membrane is intensely injected, as is readily seen when the tenacious mucus is removed. The smaller bronchi are apparently in a similar condition, and may be filled with the muco-purulent secretion.

Harden a piece of lung with several of the larger bronchi in it in Müller's fluid (§ 53, p. 42), and a second in chromic acid (§ 57, p. 44), and an extremely thin section in chromate of ammonia (§ 59, p. 45), cut sections (§ 67, p. 48), stain one in picro-carmine (§ 73, p. 53), and mount in Farrant's solution (§ 98, p. 71). Another section should be stained in logwood (§ 74, p. 56), and mounted in Canada balsam (§ 96, p. 69).

Examine first under a low power (× 50), and note that next the lumen there is an apparently cellular layer, consisting principally of small round cells, with here and there one rather more elongated, generally placed at right angles to the surface of the mucous membrane. Beneath this is the basement membrane, which is enormously swollen, and is hyaline and œdematous looking. Immediately beneath this, and apparently pushing their way for some distance into the basement membrane, are numerous distended blood-vessels, which lie principally in the inner fibrous coat of the bronchus. Around the vessels, and separating the fibrous laminæ, are numerous corpuscles, recognised under this power as deeply stained (pink) granules. They are especially numerous around the vessels, but are

to be met with throughout the greater part of this inner fibrous layer. In the same way the muscular coat may contain a few of these cells, whilst the outer fibrous coat often, though not invariably, also appears more cellular. This peribronchitis is usually not a very marked feature in the acute form of the disease. The catarrhal changes are the most prominent, and as this is perhaps the best position in which to observe them, a short *resumé* of the process is given.

For such an examination the high power (× 300) must be used. Within a few hours of the commencement of the attack, the blood-vessels in the inner fibrous coat are distended, as already seen, pushing in the basement membrane towards the lumen of the tubule. In from sixteen to twenty-four hours the basement membrane becomes swollen and œdematous looking, and this change is followed almost immediately by a separation of the ciliated and columnar epithelium, which at this stage may, on microscopic examination, be found in the frothy expectoration. After this the cells do not again become columnar until the mucous membrane returns to the healthy condition. Along with this there are marked changes in the mucous glands, the cells of which first undergo cloudy swelling, and then secrete mucus more actively, so that the clear goblet-like cells are very numerous, and in the centre of the gland there is a considerable amount of granular-looking material. After a few days the typical catarrhal condition is met with. Debove's layer of flattened cells is seen lying on the swollen basement membrane, whilst above these flattened cells are numerous rounded or peg-top shaped cells, which are evidently derived by proliferation from the cells of Debove's layer. As these cells become detached, they, along with the mucus from the active glands, constitute the muco-purulent discharge, the greyish parts being composed of mucus, the yellow or purulent material being composed of the separated round cells. The changes in the inner fibrous coat are chiefly around the blood-vessels, which are distended, and surrounded by a number of leucocytes and young connective tissue corpuscles, which take on carmine and logwood staining very readily. Extending into the muscular coat are similar masses of round deeply stained cells, and it is to the presence of these cells, as a result of inflammation, that the weakening of the muscular coat is due; and, as in the case of blood-vessels, as soon as the muscular

coat is involved, there is dilatation of the bronchus and bronchiectasis. The outer fibrous coat is usually involved only as the disease becomes more chronic, when there is extreme cellular infiltration. In the medium sized bronchi the changes are much the same, except that there are no mucous glands present, and consequently no mucus.

Chronic Bronchitis.

186. Chronic bronchitis usually occurs in older people who have been subject to the more acute form of the disease during earlier life. On examining a lung from such a case, the most marked feature is emphysema, the free margins of the lungs are very much distended, and the other characters of this condition are recognised.—(See Emphysema, § 188, p. 249). On squeezing the cut surface, a quantity of muco-purulent discharge is expelled from the bronchi, which, on examination under the microscope, is found to be composed principally of small round cells. Slit open a bronchus, and note that the mucous membrane is deeply congested, and is usually of a dark red colour, and except that it is thrown into longitudinal folds, it is smooth and glistening in appearance. The smaller bronchi are usually dilated, and stand out more prominently than normal.

Under the low power (× 50), note that the bronchial wall is greatly thickened and extremely granular, especially around the distended blood-vessels, the cartilages are not so prominent as in the normal bronchus, and the muscular coat is almost obscured. Lining the bronchus is a layer of cells, but they are rounded, or peg-top shaped, and very seldom columnar.

Under the high power (× 300), examine first the epithelial cells lining the wall of the bronchus. These consist simply of rounded or incompletely developed columnar cells, and are very similar to those met with in the later stages of the acute form. The basement membrane is swollen and homogeneous looking, whilst its under surface is recessed at points by the pushing in of the vessels of the inner fibrous coat. These vessels, however, never come to the surface of the basement membrane. The small round cells in the inner fibrous coat vary slightly in size; the smaller ones are simply exuded leucocytes, whilst the larger ones are derived from proliferation of the connective

tissue cells. These do not pass to the surface of the basement membrane, though a few may be found around the vessels in its deeper part. The cartilages are shrivelled and atrophied in appearance, as are also the muscular fibres, and they are evidently undergoing atrophic changes, due to the great increase in the number of the deeply stained round cells.

In the outer fibrous coat, and extending along the lines of the interalveolar, and even the interlobular septa, there is a similar new cell formation extending around the bronchi for some distance in this way, giving rise to a kind of interstitial pneumonia. These changes are most marked along the lines of the bronchial vessels and lymphatics, extending from them to the lymphatics of the surrounding tissues.

Capillary Bronchitis.

187. This is usually met with in broncho-pneumonia, and is frequently a result of the more acute form of inflammation, probably not by an extension of the inflammatory process, but rather by the application of the catarrhal products directly to the mucous membrane, or by the formation of a small plug of secretion in the bronchus; or more probably still, it only occurs in connection with the broncho-pneumonic process. The changes are really those of bronchitis, peribronchitis, and catarrhal pneumonia, accumulation of catarrhal cells in the bronchi, proliferation of the epithelium, swelling of the basement membrane, dilatation of the bronchus, peribronchial small cell infiltration, which infiltration extends to the interalveolar septa. This process is so closely related to broncho-pneumonia, that the other changes may perhaps be best studied under that head.

Emphysema of the Lung.

188. As seen in chronic bronchitis and in old persons, emphysema is said to be atrophous, whilst the emphysema met with in broncho-pneumonia along with collapse of patches of lung tissue is spoken of as compensatory emphysema. It may also be divided into (1.) vesicular emphysema, in which there is simply dilatation of the larger air cavities; and (2.) interstitial emphysema, in which the air has passed from the proper cavities into the surrounding or inter-

stitial tissue. Of the latter form it is necessary to say little, except that to the naked eye the change is observed along the lines of the interlobular septa, in which a number of small air-filled spaces make their appearance. These small spaces are never of any great size, but they form a kind of beaded line running from the free margins of the lung for some distance under the pleura, or even between individual lobules. This form appears to be an extension of the vesicular process, or it may be due to rupture of air vesicles, or of a wound in the larger air passages or in the pleura, &c.

Vesicular Emphysema.

189. This is usually met with where there is altered nutrition of the lung tissue, so that the air cavities are more easily dilated. It is therefore specially common in chronic wasting diseases, in chronic lead poisoning, and in old people. In addition to these predisposing causes, however, there must be a direct or exciting cause, as the coughing in the case of old people who are suffering from chronic bronchitis, or in the case of children (where the coughing is the chief cause) in whooping-cough, where there is forced expiration, with closure of the glottis during coughing. This, when continued for any length of time, gives rise to the emphysematous condition. The causes are, then, long continued and often repeated high pressure in the air cavities, accompanied by weakening of the walls of cavities by impaired nutrition.

Naked eye characters.—On opening the chest cavity the lungs are found to be considerably more voluminous than normal, the anterior margins of the lung extending much further than they usually do—in some cases overlapping—when the sternum is removed. The organ is light, and may weigh several ounces less than a healthy lung. The whole of the outer surface appears deep in colour, except near the apex, down the anterior margins, and around the margin at the base, where there is a greyish pink colour. At these points the outlines of the lobules are not so distinctly visible, but when made out they show that the lobules are considerably increased in size. There is great distention of the lung tissue, and what are called emphysematous bullæ are formed. Here the tissue appears to be light and spongy,

and feels almost like a mass of feathers in a silk bag. Squeeze the dilated portion, and it will be observed that the air can be driven from one point to another along the margin of the lung; and if a single incision is made, the air in the whole of the emphysematous portion may be driven out at the one opening. The tissue "cuts" with a peculiar gritty or harsh feeling, and to the touch the cut surface feels harsh and dry. Throughout the whole of the non-emphysematous part of the section there is more blood than one meets with in the healthy lung. On examining the cut bullæ they are found to consist of large cavities, across which run thin non-vascular trabeculæ, evidently the remains of interalveolar septa. No blood oozes out from the section where the bullæ are well marked; on squeezing the lung a yellow catarrhal fluid exudes from the bronchi, as in this condition there is bronchitis usually of old standing.

With a piece of string tie one of the emphysematous bullæ firmly, so as to keep in the air. Remove the mass below the constricted portion. To the string attach a weight sufficient to sink the mass. Place in Müller's fluid (§ 53, p. 42) or chromic acid (§ 57, p. 44), cut sections (§ 67, p. 48), stain in picro-carmine (§ 73, p. 53), and mount in Farrant's solution (§ 98, p. 71).

Under the low power (× 50) all the changes are seen to be most marked immediately under the pleura. Instead of the angular and polygonal openings of air cells, the openings are round, and are somewhat increased in transverse diameter. It will be noted, however, that these smaller rounded openings are much fewer in number than are the polygonal openings in the healthy lung. In place of a number of them there are large irregular openings, usually surrounded by cup-shaped depressions. Where there is a favourable section the capillary blood-vessels are seen to form a network, with wider meshes than in the normal lung, and the transverse diameter of the vessel is not so great. The vessels are apparently stretched over an expanded surface. Although there is evidently dilatation, and probably thinning of the walls, this is not at first sight apparent, for the sections of the walls between the individual cavities are sometimes even broader than in the normal lung. This may be thus accounted for:—In emphysema the individual air cells are not distended; there is rather a distention of the infundi-

bula and the alveolar passages, and, as a result of this distention, a flattening out of the air vesicles, which are situated at the margin of

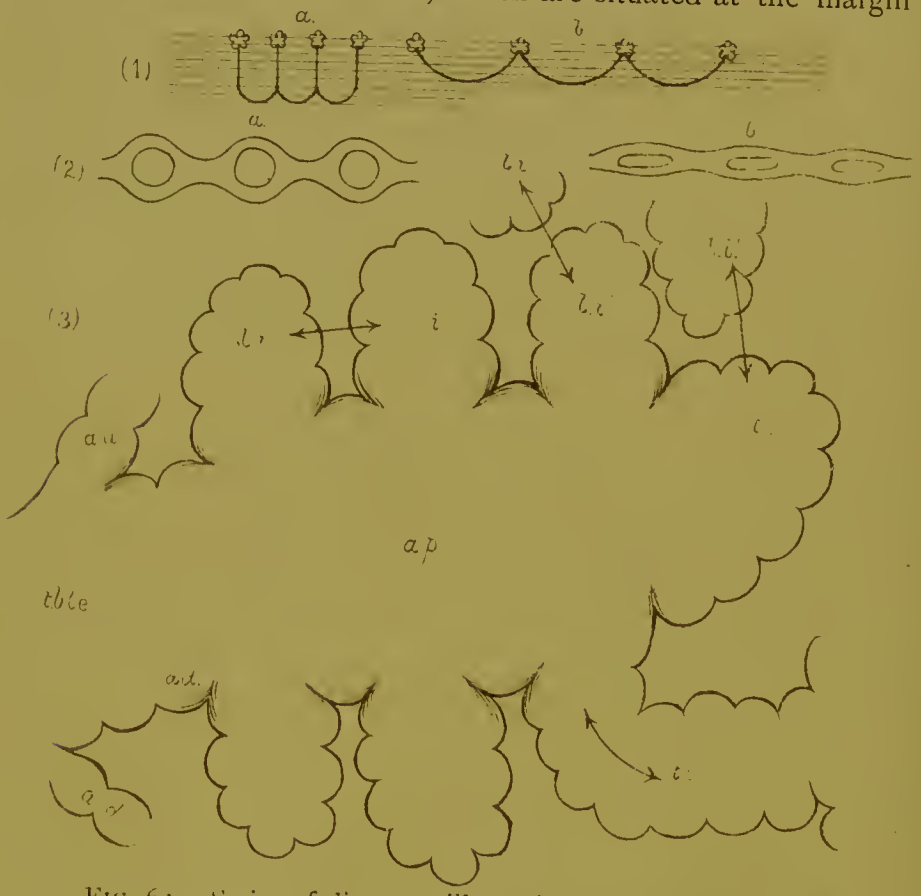


FIG. 63.—Series of diagrams illustrating the changes which take place in emphysema.

(1.) *a.* Normal air vesicles through which a series of imaginary sections are made at right angles to the wall.

b. Air vesicles flattened out, and sections therefore pass obliquely through their walls.

(2.) *a.* Sections of capillaries in normal lung.

b. Sections of compressed capillaries in emphysematous lung. The pressure is due to the flattening out of the air vesicles.

(3.) *a.p.* Dilated alveolar passage.

Infundibula terminal, *l.i.*, and lateral, *l.i.*, dilated, air vesicles flattened.

l.i[1]. Terminal, and *l.i*[1]. lateral infundibula of other alveolar passages into which ruptures indicated by double arrows take place; between *l.i.* and *l.i.*, infundibula of the same alveolar passage, rupture may also occur.

t.b.le. Terminal bronchiole.

a.d., *a.d.*, *a.d.* Alveolar ducts.

Hypertrophied muscular tissue at mouths of infundibula &c., is indicated by shading.

these, and the greater the distention of the larger cavities the more marked becomes the flattening of the air vesicles, the walls of which

also become considerably stretched. Consequently, if the normal air vesicle be imagined as represented by a cup with a thickened rim, the embryonic epithelial cells, &c. at the edge of the cup forming this rim, the flattened out emphysematous air vesicle may be compared to a saucer, also with a thickened rim. If the cup be cut down in transverse sections, a considerable number—say eight or ten—are cut almost at right angles to the septa, and therefore in a direction showing least thickness of the wall. In cutting down the saucer, on the other hand, the number of sections must be fewer—only two or three—and each section passes obliquely through the wall, which consequently appears thicker, though it may actually be thinned, and the relative, but not the absolute, number of sections through the bottoms of the concavities will be increased. Hence the apparent thickening of the walls of the spaces and the numbers of membranous patches over which the capillary vessels are stretched. It will be remembered that when the section was made into the lung there was in the emphysematous portion no exudation of blood, even on pressure—this being due to the fact that the pressure on and distention of the vessels frequently bring about their occlusion. By this fact, too, is the absence of hæmorrhage after rupture of the septa during life accounted for. The breaking down of the septa does not take place irregularly, but follows a regular plan. The septa between individual air cells never give way, they are simply stretched out; but the septa between adjacent infundibula of the same alveolar system, or between infundibula of adjacent alveolar systems, may be broken down. These changes will perhaps be better understood with the aid of a diagram.

Under the high power all the above appearances should be verified, and in addition there are a few fibres of muscular tissue to be observed around the openings of the infundibula. In emphysema these are more distinctly seen than in the normal lung, as they are somewhat hypertrophied. Besides the changes in the walls already noted, there are marked changes in the epithelium lining the air vesicles. It is granular and atrophied, and is evidently undergoing fatty degeneration. (Stain a section in osmic acid, § 80, p. 62.) These atrophic changes are brought about by the constriction of the capillary blood-vessels—the greater the constriction, the greater the amount of fatty degeneration and atrophy of the epithelial cells.

Another change brought about by the obliteration of the capillaries is thickening of the walls, and even atheroma of the larger branches of the pulmonary artery. (See § 147, p. 156).

In this condition the right side of the heart is usually dilated, and also somewhat hypertrophied.

Collapse of the Lung.

190. This is met with under three or four different conditions.

(1.) It may be met with in patients who, before death, have been extremely exhausted, and where there has not been sufficient strength left to enable the patient to take a full inspiration. In such cases the collapse is in the lower and posterior, or least moveable, portions of the lung. The tissue has a firm and fleshy feeling, is non-vesicular, and sinks in water. In this form there is usually congestion of the collapsed and surrounding parts.

(2.) In weakly new-born children there is a similar condition, known as *atelectasis*, where the collapse occurs in conoidal patches of one or more lobules at the periphery, especially near the root and at the base of the lung. The collapsed patches in such a condition are of a bluish or slate colour, and the tissue is so solid that it sinks in water.

(3.) Where there is an effusion of fluid into the pleural cavity, as in pleurisy, there may be collapse of the whole lung. This may disappear if the fluid is absorbed; but where at the same time there is a thickening of the pleura, and organisation is taking place in the lymph, the lung may be bound down to the postero-internal wall of the chest, and the collapse remains. The lung is anæmic at this stage, though it may be somewhat œdematous.

(4.) Collapse may also be due to a wound in the chest wall in which the visceral pleura is involved. Here the lung is first congested and solid, but after a time it may become more anæmic than the other lung, which, however, in such circumstances, has a tendency to become congested and even emphysematous.

In all the above forms the tissue feels firm and fleshy, there is no crepitation, and no air can be squeezed out on pressure; a part of the solid lung will sink in water, and though in the earlier stages of collapse the lung is congested, in the later stages it becomes anæmic, as its function is in abeyance.

(5.) Lobular collapse takes place in broncho-pneumonia, under which heading it is described as leaden looking patches, frequently depressed below the surface of the surrounding lung. This form of collapse is usually determined by a plug of mucus which acts as a ball valve, allowing air to pass out, but falling back to the mouth of one of the smaller openings at the bifurcation of a bronchus whenever air enters the lung. It is accompanied by congestion of the capillary vessels of the collapsed parts, and by emphysema of the lobule supplied by the corresponding smaller branch of the bronchus, which is not plugged. It is usually situated at the base and posterior border of the lung, but large depressed patches may be present at almost any part of the surface.

Catarrhal Pneumonia.

191. Synonyms, "Broncho" Pneumonia, "Lobular" Pneumonia.

This condition, in its simplest and most typical forms, is met with in children who have suffered from capillary bronchitis during the course of some of the exanthematous fevers or whooping-cough. It is also met with in hypostatic pneumonias, where the contents of the alveoli are to a great extent catarrhal, though the distribution of the process is lobar, not lobular. If a lobular catarrhal lung is examined during the earliest stage of the disease, it will be found that there is seldom any extensive pleurisy, in which respect this form differs from the lobar form, in which pleurisy is a well-marked feature. On the surface of the lung, which usually appears somewhat congested, are seen a number of firm, solid purple patches, varying in diameter from one-tenth of an inch to one-fifth of an inch. These are angular in shape, and are frequently retracted slightly below the surrounding surface (collapsed lobules). In addition to these, there are a number of patches of similar appearance and consistence, which usually project beyond the surrounding surface (the pneumonic patches). Around each of them the interlobular septa may be distinguished, and the lobules in the immediate neighbourhood appear to be distended with air, and in some instances they are almost in a condition of emphysema. On section, the lung is found to be markedly congested throughout; the small angular

patches coincide in extent with the lobules, and near the surface they are of a pyramidal shape; the solid patches are not very sharply defined from the surrounding tissue, are smooth and non-vesicular, and very little fluid can be squeezed out from them; the surrounding dilated air vesicles stand out very prominently, and their walls evidently contain a considerable amount of blood, as the tissue presents a very congested appearance to the naked eye, and both blood and air may be squeezed out from this part of the lung in considerable quantities.

Either during this stage, or more frequently during the next, the solidified and purple pneumonic patches may run together, and so form a solid mass, involving a considerable part of a lobe of the lung. A careful examination in such a case is necessary to enable one to say that it is not a condition of acute or croupous pneumonia. If it be remembered, however, that in broncho-pneumonia the solid mass is made up of a number of small solid patches, and that consequently the outline is likely to be irregular (as is the case), the diagnosis becomes comparatively easy. In addition to this irregularity of the outline, there are usually a number of lobules and smaller patches which have as yet not become fused to the main mass.

Examine the bronchi in this lung, and note that the larger ones are deeply congested, whilst in the smaller ones there are marked evidences of acute catarrh, and on squeezing the lung a quantity of muco-purulent material is pressed out from the bronchial tubes. Between the solid looking patches, which are not granular, the lung tissue, though usually deeply congested and emphysematous, is normal.

Harden a piece of this lung in Müller's fluid (§ 53, p. 42) or chromic acid (§ 57, p. 44). Stain a section in picro-carmine (§ 73, p. 53), and mount in Farrant's solution (§ 98, p. 71).

Under a low power (× 50) examine a single lobule in which the catarrhal pneumonic process has been detected with the naked eye. In the centre of the lobule is the small bronchus, recognised as a large rounded tube, with thickened granular looking walls. In this tube there are usually a number of small cells, which are recognised under this power as small granules. Near the bronchus runs the branch of the pulmonary artery, known by the thickness of the

adventitia and the quantity of pigment deposited in its lymph spaces.

Immediately around the bronchus the air vesicles are filled with a mass of delicate fibrils and cells, a mass which, compared with the exudation in the red hepatization stage of croupous pneumonia, differs only in the fact that it contains a greater number of cells. It remains semi-transparent when stained with picro-carmine, and completely fills up the alveolar cavity. Where this process is not of long standing the walls of the alveoli are thickened from distention of the blood-vessels, and a number of larger cells are usually found situated near the wall of the air vesicle. The fibrinous exudation above described is confined to a very small area immediately around the bronchioles and the branch of the pulmonary artery. Outside this zone the air vesicles are filled with a mass of catarrhal cells—cells of considerable size, and with little or no fibrin between them. These, or their nuclei, are deeply stained, and in this area the tissue is not nearly so transparent as in the central zone. Here, too, the capillaries in the walls of the air vesicles are distended. The catarrhal change may extend to the periphery of the lobule, but in many cases there is an outer zone in which there is merely congestion of the capillary vessels, accompanied by slight proliferation or detachment of some of the alveolar epithelial cells.

Examine the interlobular septa, and observe that they are more prominent than normal; they are swollen, and their vessels are considerably distended, whilst around the vessels small cells are frequently seen. The deep layer of the pleura is in a similar condition, and in it small greenish patches (composed of red blood corpuscles) are seen. These are small hæmorrhages.

The bronchi are found to be in a condition of inflammation.—(See Bronchitis, § 185, p. 246.)

Under a high power (× 300), first examine the plug of muco-purulent material in the lumen of the bronchus. It is composed principally of small, almost purulent looking, cells, and on the addition of acetic acid to the section, several small nuclei appear in each cell. The epithelium of the bronchus is proliferating, and is frequently seen only as a layer of irregular or flattened cells lying on the basement membrane; beneath this the vessels of the bronchial mucous

membrane are distended, and around them and in the peribronchial tissue there is a great increase in the number of small round pink-stained cells. This condition of infiltration of the walls with small round cells extends down to the minute bronchioles, the walls of which are in many cases extremely thickened.

The air vesicles in the central zone are filled with a more or less fibrinous exudation. It is composed of clear unstained strands of fibrin similar to those described in croupous pneumonia (§ 181, p. 233). Here, too, are seen a number of corpuscles, which, however, differ considerably in size. (1.) Small rounded corpuscles with a double outline, stained green with picro-carmine—red blood corpuscles: (2.) Corpuscles a little larger than the above, somewhat granular in appearance, and stained pink with picro-carmine—colourless blood corpuscles; and (3.) The third form of corpuscle is found in greatest numbers towards the periphery of the mass of exudation. It is usually very much larger (two to six times) than either of the preceding forms, and is recognised by the fact that it has usually one or several well-marked and deeply stained nuclei. The cell is rounded or oval, and is composed of delicately stained granular protoplasm, in which the nuclei stand out as deeply stained bodies. The nuclei vary considerably in size, even in the same cell. Though most of the large cells are lying free near the edge of the alveolus, some of them may be seen still adherent to the wall, and these seem to be in a state of active proliferation, some of the cells being still attached to the parent cells by bands of protoplasm only, which act as peduncles until the cells are set free. The ovoid cells are all derived from the epithelial lining of the alveoli by this process of proliferation. It is a catarrhal proliferation of the epithelium lining the air vesicles.

In the zone outside the above the air vesicles contain only the cellular elements with a small quantity of granular matrix (mucin, &c.). Here the coloured blood corpuscles and the fibrin appear to be absent. The cells are almost entirely catarrhal, and their characters, as described above, are much more readily discerned. On the addition of acetic acid the mucin between the cells may be brought out slightly more prominently, but it is always a difficult matter to observe the intercellular material. If this zone be examined in the very early stage of the catarrh, the proliferating process may be exceedingly well

observed, and the cells lining the air vesicle are seen to be swollen, multinucleated, and in many cases dividing, so that the catarrhal cells are to be observed in all stages of detachment from the alveolar wall. Where this is taking place the blood-vessels are distended, and there is slight thickening of the alveolar wall quite apart from the increased thickness of the epithelial layer. In what has been described as the outer zone, this proliferative layer of epithelium and the distention of the blood-vessels may be all that is present, though in other cases the catarrhal products fill the cells to the margin of the lobule. It will be noted, even where the catarrhal process has been going on for a few days, that the large detached epithelial cells are becoming more granular, less deeply stained, and studded with small highly refractile bodies. If a section at this stage be stained with osmic acid (§ 80, p. 62), these refractile bodies are blackened, this pointing to the fact that the cells are undergoing fatty degeneration. The interlobular septa, as already seen, are considerably thickened, the vessels running in them are distended with the coloured corpuscles (stained green with picro-carmine), and there may be small extravasations around the vessels, in addition to which there appears to be proliferation of the connective tissue corpuscles, and an exudation of leucocytes. The strands of fibrous tissue of which a septum is composed are somewhat separated from one another, and in the lymphatics granular looking masses may frequently be observed. The deeper layer of the pleura is usually in a similar condition.

The form above described is the first stage of the acute form, but it is to be remembered that, just as in the case of the croupous pneumonia, the catarrhal products may pass through a series of changes, owing to which changes both the naked eye and microscopic characteristics are somewhat altered, so in this form the various stages are described under the terms of red and grey splenization and resolution, corresponding to the stages of red and grey hepatization and resolution of the croupous form.

Grey Splenization.

192. Grey splenization corresponds very closely to the grey hepatization of croupous pneumonia.

On naked eye examination the lung is not nearly so deeply congested, and in some cases may appear, as a whole, even paler than normal, though this is due to the pallor of the more solid patches. In the centre of the solid patches there is frequently a greyish point, or the grey colour may be marked throughout the whole lobule. On palpation, the patches feel soft and almost fluid.

Make a section into the lung, and note the slight congestion around the greyish green or greyish yellow lobules. Then squeeze the lung, and note that from the bronchi, even the very small ones, a quantity of muco-purulent material is exuded: this, on microscopic examination, is found to consist of pus corpuscles, or of fat globules of various sizes, which are blackened by osmic acid. On the addition of acetic acid, this material becomes stringy, from the mucin it contains. The mucous membrane of the bronchi is deeply congested.

Harden a piece of a lung in this condition in Müller's fluid (§ 53, p. 42), and a second in chromic acid (§ 57, p. 44). Stain a section in picro-carmine (§ 73, p. 53), and a second in osmic acid (§ 80, p. 62).

Examine under the low power of the microscope (× 50), and note that the exudation in all the zones of the lobule is broken down, and that, in place of the catarrhal cells, smaller pus cells and large granular corpuscles are seen in considerable numbers; these, when stained, are dirty brown and opaque, or with the osmic acid they are almost blackened.

On examination under the high power (× 300) the pus cells and compound granular cells are seen very distinctly at the centre of the air vesicle, whilst at the margin there are usually a few small flattened epithelial cells growing, and forming a lining for the air cavity. The other appearances are much as in grey hepatization of the lung (§ 182, p. 237).

Later, the microscopic appearances are much as in the stage of resolution in croupous pneumonia: the whole of the catarrhal products are broken down and softened; they form a fatty pultaceous mass, part of which is expectorated, and part is absorbed by the lymphatics, and, in a section stained with osmic acid, the fatty material may be traced in the absorbents in the interlobular septa.

The epithelium is regenerated during this stage, and is seen first as a layer of cubical cells lining the air vesicle, and in the interalveolar septa there is some increase in the number of connective tissue corpuscles.

Here, as in the case of lobar or croupous pneumonia, it is impossible to go into all the forms of disease which may follow acute catarrhal pneumonia, but the following more common sequelæ may be mentioned, as given by several writers.

Sequelæ.

193. (1.) Acute suppurative broncho-pneumonia, in which the pneumonia is set up by retained bronchial secretion. This condition is so acute, and the infiltration of the tissues around the bronchus with colourless blood corpuscles is so great, that an abscess is formed, which may involve the whole of the tissue in the immediate neighbourhood of the bronchus. To the naked eye, the lung presents the characteristic features of ordinary lobular pneumonia, with here and there points of suppuration.

(2.) Chronic broncho-pneumonia, which appears to be little more than an interstitial pneumonia, set up by the irritation of the absorbed broncho-pneumonic products. It occurs as a diffuse form especially in children, and as a nodular form in old people. The appearances, both naked eye and microscopic, are very much those of interstitial pneumonia (described in § 196, p. 271).

(3.) Caseous broncho-pneumonia, of either the nodular or the diffuse form, is as yet not exactly localised; by some it is placed in the class of true catarrhal pneumonias (see papers by D. J. Hamilton in the *Practitioner* for 1879, *et seq.*), whilst by other authorities it is referred to the specific or tubercular diseases. To whichever class it may belong, it will be more conveniently treated under the heading of phthisis than under broncho-pneumonia.

(4.) Owing to the changes in the walls of the bronchi in broncho-pneumonia, a form of ulcerative bronchiectasis (of the small lobular bronchi) is sometimes met with, in which irregular cavities containing softened or purulent material are seen. This form is apt to be mistaken for caseous tubercle (Greenfield).

The Pneumono-Konioses, or the Dust Diseases of the Lung.

The most important of these are—

1. Anthracosis—Coal-miners' phthisis.
2. Siderosis—Needle-grinders' phthisis.
3. Silicosis—Stone-masons' phthisis.

But there are numerous other forms such as those, due to inhalation of vermilion, wool, cotton, &c.

Of these it will be necessary to examine specimens of the first and third only, in both of which, however, characters distinctive of the special disease or of the group may be observed.

"Anthracosis," or Coal-Miners' Phthisis.

194. If the lung of a coal-miner be examined, it is invariably found to be intensely pigmented; but in stone-masons' phthisis there are certain additional and very characteristic features. The lungs are found to fill the pleural cavity more completely than in the normal condition, and are usually adherent at points to the walls of the chest; they are of greater size and weight, are found to be considerably firmer, and more solid than a normal lung. On examining the pleural surface, it at first sight appears to be uniformly black, but on closer examination small dark spots, or accumulations of pigment, from which lines radiate in various directions, may be seen, these lines corresponding to the lines of the lymphatics of the interlobular septa. Very frequently in the centre of these spots there is a lighter coloured point. These spots, with their light coloured centre and the dark ring outside, are found to be firm, hard, and fibrous feeling, and are about the size of a mustard seed, or a little larger. On making a section into the lung, it is found to be firm and tough, and has a peculiar harsh emphysematous feeling, whilst small nodules similar to those seen on the pleural surface are scattered throughout the substance of the lung, but in smaller numbers; they have the same hard fibrous consistence. Between these nodules the pigmentation is not nearly so well marked, though it will be observed that even here there is a considerable deepening of the colour of the tissue, especially along the course of the lymphatics in the interlobular septa.

From the cut surface a large quantity of inky black fluid may be pressed out, which in the fresh condition stains the hands. The bronchial glands when incised are found to be firm, hard, and deeply pigmented. The mucous membrane of the bronchi is pink (not black), and is covered with mucus; it is often considerably injected. At one or two points in the lung, if the disease be far advanced, the lung tissue presents the appearance of a solid black mass, or in the blackest part of this there may be a cavity bounded by ragged sloughy looking walls.

Harden the lung in Müller's fluid (§ 53, p. 42), or chromic acid (§ 57, p. 44).

Low power (× 50).—Examine the section, on which should be a piece of the pleura, and which should comprise sections through several lobules.

Note that the pleura is divided into two distinct layers; the more superficial of which is scarcely pigmented at any point. It is in fact apparently little changed. Between it and the deep layer is a sharp line of demarcation, and this deep layer, which is considerably thickened, sometimes being three or four times the normal thickness, is reached at once. Throughout the thickened pleura are to be observed black patches, which evidently follow the lines of the lymphatics in the connective tissue, and surround the blood-vessels; they are sharply bounded by the walls of the lymph spaces or sinuses.

The interlobular septa continuous with the deep layer of the pleura are also considerably increased in size, and the lymphatics are similarly injected with this coal-black pigment. From the interlobular septa the black lines and masses may be traced into the perivascular and peribronchial tissue, as the lymphatics surrounding these tubes are in direct communication with those in the septa, and so with those in the deep layer of the pleura. The mucous membrane of the bronchus is entirely free from pigment of any kind, though it is frequently swollen and otherwise changed.

Having examined the coarser masses of pigment, next note carefully the interalveolar septa, which even under this low power appear to be considerably thickened, and in the thickened walls of the air vesicles are seen numerous dark-coloured patches. Near one of these patches observe the appearance presented by an air vesicle.

There is evidently swelling and proliferation of the epithelial cells, some of which appear to contain particles of the coal-black pigment, so that under this power the air vesicles contain a number of detached cells, many of them deeply pigmented, but others seen simply as catarrhal cells, derived from the epithelial surface. If a small branch of the pulmonary artery is examined, it will be found that, in addition to the thickening of the outer coat or adventitia, there is also an increase in the thickness of the intima, leading in many cases to a decrease in the size of the lumen of the vessel, or in some cases to a complete obliteration of the vascular tube. This is especially well marked where the nodules are most numerous, and it appears probable that the fibrous nodules have in their centre, very frequently at any rate, an obliterated vessel. It is also found that where these nodules are most numerous the process of breaking down is most marked, due possibly to the obstructions of the lymphatic and blood flow.

High power (× 300).—Here examine the tissues in a different order. Follow the course of the pigment in the lung. In the mucous membrane of the bronchi no pigment is found, but frequently there is proliferation of the epithelial cells, many of which in such cases are but imperfectly ciliated, are not so well formed, and are, as a rule, much smaller. Lying beneath these cells is a more or less homogeneous membrane, swollen and œdematous, whilst the vessels beneath are somewhat congested. There is, in fact, in such cases a condition such as will be described under the heading of bronchitis. The pigment, whatever may be the reason, does not effect a lodgment on the mucous surface of the bronchus, In the air vesicles, however, coal particles are found in considerable numbers, some of them lying free on the surface of the epithelium, others contained within epithelial cells detached from the epithelial layer, whilst others again are found within swollen epithelial cells, still attached to the wall of the air vesicle. In addition to these are found numerous nucleated cells lying free in the cavity. Such cells vary from the size of a colourless blood corpuscle to three or four times that size, and some few of them may have several nuclei. Here and there, too, are seen a few coloured blood corpuscles, recognised by their small size and double outline.

In the walls of the air vesicles under this power marked changes may be seen. The lymphatics or lymph spaces in many cases appear to be packed with pigment. If the connective tissue cells in the walls of these spaces be carefully examined, they, too, are seen to contain small granules of coal-black pigment, and some free cells lying in the lymphatic channels also hold pigment granules. In this position there is evidently considerable proliferation of the connective tissue corpuscles, for nuclei are much more numerous than in the normal lung, and there is also a great increase in the amount of fibrillated tissue around the capillary vessels. The capillary vessels are usually considerably dilated and distended with blood corpuscles. In some few cases small fibrous nodules are formed in the interalveolar septa, but this does not occur very frequently. Similar changes on a larger scale are found in the interlobular septa. The lymphatics are marked out by the deposition of pigment within them; there is considerable increase in the amount of interstitial or connective tissue, many of the cells containing the granules of carbon, and the blood-vessels are distended, or, in some cases, though filled with blood, are considerably contracted, owing to thickening of both the intima and the adventitia. In this position the fibrous nodules are frequently met with. They are pale and fibrous looking in the centre, but towards the periphery they contain, in the spaces between the bundles of fibrous tissue, a considerable quantity of the same black material. From the alveoli, near the surface, the pigment is carried by the more superficial lymphatics of the interalveolar and interlobular septa to the deep layer of the pleura, where, as already seen under the low power, the thickening and pigmentation are extremely well marked; and all the changes observed in the interlobular septa may be seen in this deep or subpleural layer. The superficial layer of the pleura is comparatively unaffected; there is no marked pigmentation, and but little increase in the thickness. The lymphatics of this layer, therefore, do not communicate with those of the layer beneath.

From the lymphatics surrounding the alveoli nearer the root of the lung the pigment is carried to the perivascular and peribronchial lymphatics, giving rise to changes similar to those described as occurring in the above situations.

In the perivascular lymphatics, or those around the branches of the pulmonary artery, the masses of carbon pigment are especially numerous. Here they act as irritant bodies, and set up proliferation, as in other parts, so that eventually the fibrous nodules are formed around the vessel. Then, endarteritis setting in, layer upon layer of proliferated flattened cells (derived from the flattened cells lying directly in contact with the blood current) is formed, until, in some cases, the lumen becomes obliterated, and a solid fibrous nodule remains, which in time may undergo degenerative changes, soften and break down in the centre, leaving a small cavity, bounded by rugged, fibrous, blackened walls. Around the bronchi the changes are not so marked, but even here the fibrous tissue may be invaded, but never the mucous membrane proper. To sum up: the small black nodules may be found in the interalveolar and interlobular septa, in the deep layer of the pleura, and in the perivascular and peribronchial tissue. Pigment is found in all these positions, and also in the air vesicles, either lying free or contained within the proliferating epithelial cells.

"Silicosis," or Stone-Masons' Phthisis.

195. "*Lithicosis*," *&c.*—In all essential details this process is similar to the condition of anthracosis; but owing to the greater irritation set up by the stone particles, the course of the disease is much more rapid, and the proliferative and destructive changes are induced in a comparatively short time and in much graver forms than in anthracosis. The clinical history is largely that of ordinary phthisis, but the pathological process is quite distinctive. This form of disease is especially met with amongst stone-masons and quarrymen who work in dry silicious stone, where the dust particles are very fine and are therefore readily inhaled.

Naked eye appearances.—As soon as the hand is introduced into the pleural cavity in this condition, evidences of the disease present themselves. Over the surface are patches of adhesion in different stages of organisation, but most of them exceedingly tough and fibroid, and it is often necessary to strip away the costal pleura in order to get out the lung. The pleura is considerably thickened.

The organ feels firm throughout, but the surface is studded with small, hard, fibrous nodules, about the size of a split pea (larger than those seen in anthracosis), which on further examination have a very characteristic appearance.

The centre of the nodule is frequently yellowish in colour, and is surrounded by a grey, or bluish or pinkish grey, fibrous looking ring; outside this again is a pigmented zone, which in some cases is very distinctly marked. On cutting into one of these nodules, it will be found to consist of hard fibrous tissue at the periphery, with a gritty centre, the pigmented zone around this varying in size and colour with the age and surroundings of the patient. To the touch they feel like small beads scattered over the surface.

On section of the lung, numerous nodules are seen scattered regularly throughout the tissue. Between the firm, fibrous, or gritty nodules there appears to be a great increase in the amount of interstitial tissue, which becomes so marked in certain cases that the lung feels almost like a mass of cirrhotic liver. Bounded by the fibrous bands are numerous large cavities (bronchiectatic cavities), which have a characteristic shape and appearance; they are pyriform in shape, the apex of the cavity usually communicates with a bronchus (of which it appears to be a dilatation), and the base is situated towards the pleural surface. The walls of the cavity are hard and thickened, and are lined by a pink, glistening, or translucent looking membrane, which is continued into the cavity from the bronchial wall. Radiating from the thickened wall are numerous fibrous bands, some continuous with the deep layer of the pleura, others with the peribronchial and perivascular tissue more deeply situated. These fibrous bands are the thickened and fibrous interlobular septa. It will be noted throughout that the fibrous nodules, although met with around the bronchi and vessels, are much more numerous and are more prominent in the fibrous interlobular septa. The septa, then, may be looked upon as the true position of the various changes. (For the nature and mode of formation of bronchiectatic cavities see § 197, p. 274). Harden a piece of the lung with pleura and a cavity in Müller's fluid (§ 53, p. 42), a second in methylated spirit (§ 52, p. 42), or chromic acid (§ 57, p. 44); cut sections (§ 67, p. 48), stain one in picro-carmine (§ 73, p. 53), and mount in

Farrant's solution (§ 98, p. 71); stain a second in logwood (§ 74, p. 57), and mount in Canada balsam (§ 96, p. 69), and mount one unstained in glycerine (§ 97, p. 70).

Examine under a low power (× 50).—It will be at once observed that there is an enormous increase in the amount of fibrous tissue. This increase occurs as before stated, more especially along the lines of the interlobular septa. In the thickened septa the rounded nodular masses are seen. They consist usually of a mass of fibrous layers arranged concentrically, the nuclei of which take on very deeply the picro-carmine stain. In the centre of the mass there is frequently a somewhat homogeneous or granular material which takes on a yellow stain; there is degeneration and breaking down of the tissue, as at this point it derives very little nutriment from the surrounding tissue. The reason of this will be immediately seen. Around the yellow centre the fibrous tissue is very evident, but it is not very vascular. Further out again there is a zone of exceedingly vascular and cellular connective tissue. At some points this appears to be little more than a mass of young rounded connective tissue corpuscles, which take on the carmine stain very readily. Throughout this the larger vessels and capillaries stand out very prominently, as they are all greatly distended with blood, and there are evidently marked changes taking place in the walls of the larger vessels. The adventitia is thickened and very cellular looking, whilst in the intima there is great proliferation of the cells. In this position, too, there are numerous cells of considerable size, most of which contain a quantity of carbon pigment. In the tissues around, *i.e.*, in the walls of the alveoli, the vessels are extremely engorged, and there is some interstitial new formation along the lines of these capillaries. In the air vesicles there is marked catarrh, the large epithelial cells containing small black granules of pigment. The air vesicles appear to be smaller, and the epithelium in them in some cases is becoming more or less cubical (*i.e.*, it is reverting to the embryonic type). In the peribronchial and perivascular tissue similar but less marked changes are found. Here it is that the pigmentation is usually the most prominent feature. The changes in the bronchi themselves are very similar to those found in coal-miners' lung.

Under the high power (× 300).—Examine the tissues in the same order. The fibrous tissue in the septa is seen to be almost fully developed, though at certain points, especially near the nodular masses, there appears to be very rapid proliferation of the connective tissue cells. The pink fibrous bands, with the elongated nuclei deeply stained, are readily distinguished in the carmine-stained specimen.

Examine the larger vessels, in which marked changes may be seen. The adventitia, in common with the surrounding connective tissue, is undergoing proliferative changes. The cells are more numerous, and this part of the coat is thickened. In some of the elongated spaces in the thickened adventitia small granules of black pigment and particles of stone may be observed; these silicious particles are usually grey in colour, especially at the margin, but the centre appears to be clear and highly refractile. In addition to the pigment in the spaces numerous large cells contain similar material. In the intima proliferative changes are also going on, and the process known as obliterative endarteritis of granulation tissue is brought about (§ 149, p. 164). In such vessels as have not yet become obliterated the lumina are filled with blood corpuscles. In the rounded nodule the centre is usually undergoing degenerative changes from the fact that owing to the obliteration of the vessels they no longer receive a supply of blood, and there is a condition almost identical with that of the caseating gumma already described (§ 120, p. 110). The nodule is stained yellow with picro-carmine, and is extremely granular in appearance. Around the yellow mass may be seen well-formed fibrous or cicatricial tissue, and it is to the contraction of this tissue that the puckering around the centre of the nodule is due. In this cicatricial tissue few, if any, vessels are visible. In some of the elongated or ovoid spaces in the fibrous tissue the black pigment granules and refractile stony particles are seen. These particles are usually unaffected by hydrochloric acid.

In the zone outside the cicatricial tissue the tissue presents simply a mass of connective tissue cells in all stages of development. Some of them are merely rounded nuclei with scarcely a trace of surrounding protoplasm. Others are more or less elongated, and have a delicate periplast, whilst others again are

fully formed connective tissue corpuscles, with a distinct, even fibrillated, periplast. In some of the cells pigment granules and silicious particles may be distinguished. Here the vessels are extremely numerous, and are very similar in appearance to those already described in the septa. It is by this zone that the tissue of the nodule is continuous with the tissue of the interlobular and interalveolar septa. The interalveolar septa are somewhat thickened (1) by the distended vessels, (2) by the increase of the interstitial tissue, in the form of small round cells (proliferated connective tissue corpuscles), and (3) by the distended lymph spaces, in which may be found cells containing pigment and stone particles. The epithelium in the air vesicles is undergoing rapid proliferation. Some of the detached cells contain the foreign particles, as do also some of those still *in situ;* but some again are undoubtedly free from any of these particles. As above seen, some of the epithelial cells are considerably more cubical than in the normal condition, and the air vesicles in this way also appear to lose part of their lumen. The changes in the interlobular septa are prolonged on to the peribronchial and perivascular tissue. Bronchitic changes similar to those met with in coal-miners' lung, but usually more acute, are to be observed. For these see section on coal-miners' lung (§ 194, p. 263, *et seq.*) For formation of bronchiectatic cavities see § 197, p. 274.

It will be observed that all the changes here are more marked and more rapid than in the coal-miners' lung, as the particles of stone are much more irritating, and give rise to greater proliferation of both epithelial and connective tissue cells, the catarrhal and fibroid changes go on more rapidly, and the changes in the vessels are more prominent and more destructive. In addition to and in consequence of the fibroid changes, the formation of bronchiectatic cavities is met with here, though not in the coal-miners' lung. The pigment granules are simply those which are met with in every lung, but by their presence in this condition they aid very greatly in localising the silicious particles.

In *siderosis*, or needle-grinders' lung, changes very similar to those already mentioned, but of a milder type, are induced.

Chronic Interstitial Pneumonia.

196. The three forms of disease above described are all forms of interstitial pneumonia, but, as already noticed, interstitial inflammation is very frequently a result of acute or lobar and of catarrhal or lobular pneumonia. It may also occur in the lungs of children affected with congenital syphilis, whilst the common form, which is also probably due to syphilis, or to tubercle, is met with in persons in more advanced life.

In the more common form, or cirrhosis of the lung (synonyms, "Fibroid" phthisis or Corrigan's lung), one lung only may be affected, or the disease may be more advanced in one lung than in the other. On opening the thoracic cavity the affected lung is found to be considerably smaller than the healthy lung. It feels firm and fibrous; the visceral pleura is enormously thickened and is firmly adherent to the costal layer, though here and there are soft fibrinous masses. The organ, on removal, feels almost like a piece of indiarubber, and it is considerably smaller than natural, whilst at some parts, especially towards the base of the lung, there may be compensatory emphysema. It "cuts" with a firm fibrous feel, and when a section is made the pleura is found to be enormously thickened, the thickening being especially well marked in the deeper layer, which is deeply pigmented, and in which small tubercular nodules may frequently be seen. In some cases, however, these nodules are absent, especially where the condition is of syphilitic origin. Similar nodules may also be found along the lines of the septa and around the bronchi. From the deep layer of the pleura firm fibrous bands pass into the substance of the lung and run to join the thickened walls of the bronchi and blood-vessels. There is often considerable pigmentation of these bands, and also of the peribronchial and perivascular tissue. The vessels and bronchi are usually crowded close together, but in addition there appears to be dilation, not of the bronchi only, but of the vessels. In the dilated bronchus there is a lining membrane, smooth, pink, and translucent looking, which is continuous with the mucous membrane of the healthy bronchus.

These dilated bronchi or bronchiectatic cavities are even more frequently met with in this form of disease than in stone-masons' lung. They are usually irregular in shape or somewhat oval, and

around the large central cavity a number of smaller sacs are placed—all communicating with the larger cavity; and these sacs, as a rule, contain a "quantity of pultaceous material, consisting of inspissated catarrhal secretion" (Hamilton).

The bronchial glands are enlarged, are frequently in a state of caseation, and other caseous or gummatous looking masses, about the size of a marble, are often found in the fibrous bands. These are especially common in the syphilitic form, but they may occur in the tubercular condition.

In several cases which have recently come under the writer's notice the interstitial changes were superseded by an acute pneumonic process, which to a certain extent masked to the naked eye the fibroid change, but in which the interstitial changes were very evident on examination under the microscope. Prepare as for stone-masons' lung (§ 195, p. 267).

To prevent useless repetition, it may be at once stated that the microscopic changes in this form of disease are very similar to those met with in stone-masons' phthisis. The thickening of the pleura is very similar to that of silicosis, as also the changes in the interlobular septa, and in the peribronchial and perivascular connective tissue. The proliferation of connective tissue takes place along the lines of the lymphatics, along which the irritant material—whether it be stone particles or specific ~~veins~~—travels. The changes in the vessels, too, are very similar—endarteritis obliterans giving rise to the gummatous-like masses in the fibrous tissue, just as in syphilitic gumma of the liver (§ 120, p. 110), and there is proliferation of the adventitia, as in stone-masons' phthisis. The air vesicles are considerably diminished in size as their walls are thickened, and the epithelium is markedly cubical, more so here than in stone-masons' phthisis. The fibrous tissue is extremely vascular towards the margins of the septa, and at the periphery of the peribronchial and perivascular tissue, where also it is extremely cellular.

Examine a section of such a lung stained with picro-carmine (§ 73, p. 53) under the low power (× 50). Note the thickening of the pleura, especially in the deeper layer. The division between the two layers is marked by the pigmentation of the deeper layer. The vessels in this position are numerous, are filled with greenish material, and

are surrounded by a number of small pink granules (nuclei of young connective tissue cells). The interlobular septa are in a similar condition very vascular, and with a large increase in the amount of cellular and fibrous (pink) connective tissue. At the margins of the septa the capillary vessels are exceedingly numerous, and appear to be those of the thickened interalveolar septa, which are becoming gradually involved by the advancing fibrous mass (§ 195, p. 268); in this region, too, there are evidences of croupous or catarrhal pneumonic processes. Other changes as above described. Find the wall of a bronchiectatic cavity, in which may be recognised some of the elements of the bronchial wall, which, however, have undergone considerable change. As already observed, there is a considerable new formation of cell elements, as a result of which the proper connective tissue may be gradually absorbed, and considerable weakening of the wall is the result. Here, too, the cartilage cells are undergoing either fatty or proliferative changes, in consequence of which the matrix gradually disappears, and there is simply a mass of small round cells left. This is a similar process to that which goes on in the absorption of the connective tissue matrix. These cartilage cells appear to be granular under the low power, but under the high power the true fatty nature may be distinguished. Further examine the lining of the cavity on which a few columnar cells, with their deeply stained nuclei, can still be made out. Running into the weakened cellular wall of the bronchus are the interlobular septa, several of them converging around each bronchial cavity.

Under the high power (× 300).—The various tissues, as above described, are to be further observed; especially the contracted air vesicles, with their thickened and fibrous looking walls, and their lining of cubical epithelium (air vesicles outside the fibrous mass are frequently somewhat dilated), the surrounding blood-vessels, the changes in the septa and pleura, and lastly, the changes in the wall of the bronchus. Any ordinary case of cirrhotic lung, syphilitic, or from whatever cause, presents most of these features in such a marked degree that there can be very little doubt as to the nature of the disease, if the examination be carefully made.

For a description of the emphysematous part of the lung, see section (§ 189, p. 250) devoted to that condition.

Bronchiectatic Cavities.

197. They have already been mentioned as occurring in stone-masons' phthisis, and in the chronic interstitial forms of pneumonia. They are found in almost all forms of chronic phthisis, where interstitial inflammatory changes are set up.

These cavities are usually of moderate size, and are frequently saccular or lobular in form, especially when they are due to the weakening of the bronchial wall by inflammatory changes, such as have been described in the two previous sections; this inflammation being set up in various ways by lymphatic infiltration, and so on.

When angular, as they are very frequently, they may be due to simple contraction of fibrous bands or cirrhotic interlobular septa. The method in which such a cavity is formed will be best explained by means of a diagram.



Fig. 64.—Diagram to represent the method of formation of bronchiectatic cavities by the traction of the cicatricial tissue in the interlobular septa on the weakened bronchial walls.

The lines *a.a.* represent the walls of the chest to which the pleura is adherent, either naturally because the cavities are air-tight, or through an inflammatory process. The lines *b.b.* are supposed to represent the interlobular septa, running first from the one wall of the chest to the wall of a bronchus, *c.*, then on to another bronchus, and lastly, to the opposite chest wall. As these fibrous bands contract, there is traction on the walls of the bronchi, and also on the walls of the chest, and as the latter are much more rigid than the former, the former have to give way at a point where the septa run into their walls. At the same time the chest wall becomes slightly flattened,

but this is not nearly so noticeable as is the change in shape and increase in size of the bronchial cavity. Here the lining membrane is smooth, glistening, and translucent, and has a pink tinge, due to its extreme vascularity.

There is another form of bronchiectatic cavity, caused by the accumulation of catarrhal products in the bronchus. This leads to distention, and the formation of a cavity of moderate size. Such cavities are usually met with in considerable numbers; they are more or less fusiform, or spindle-shaped, and have the same pink, glistening lining membrane as the above form.

Still another form of bronchiectatic cavity is that met with in ulcerative bronchiectasis following catarrhal pneumonia. In this there is ulceration of the bronchus and distension at the weakened part.

Whilst on the subject of cavities, or vomicæ, it will be as well to mention the form in which there is extensive softening of the lung tissue, as a result of various inflammatory and caseous processes. A large cavity is formed, and into this one or several bronchi open, carrying away the softened contents from the cavity. Such a cavity may usually be recognised by its greater size, the more or less irregular outline, the "several openings of the bronchi into it, and by the bands of more resistent fibrous tissue which run from side to side of the cavity" (Hamilton). These are not blood-vessels, as generally supposed, but are bands of fibrous tissue, thickened interlobular septa, &c.—very frequently, however, containing branches of blood-vessels embedded in their substance. It is now held by most authorities that these large irregular cavities are the result of the running together of several smaller cavities.

Brown Induration of the Lung.

198. Synonyms, "Brown Œdema," "Chronic Venous Congestion" of the lung. This condition is most frequently associated with disease of the valves of the heart, especially of the mitral valve, though it often occurs in connection with aortic disease.

In this form of disease the lung is usually somewhat more voluminous than natural. The pleura has a peculiar reddish purple colour, from

which deeply pigmented interlobular septa stand out very prominently. At the free borders of the lung there is frequently some emphysema, whilst in these positions, too, there often are hard, firm, deeper coloured, wedge-shaped patches, which project somewhat from the surface, and are sharply defined from the surrounding tissue. On making a section into the lung there is usually exudation of a considerable quantity of brownish red serous fluid along with a quantity of air. The general surface of the lung presents a much redder colour than normal, but it is a peculiar brownish or brick red colour, and not the arterial red colour that is met with in acute congestion. From this general red surface there is an exudation of serum, mixed with air, pointing to the fact that here the lung is œdematous. At certain points, too, there is considerable emphysema. Scattered over the section, especially of the posterior and lower part of the lung, are firmer patches varying in size from half an inch to an inch, not sharply marked off from the surrounding tissue. These are not solid, but are much firmer, harsher, and drier feeling than the surrounding tissue, and when cut into they have a peculiar gritty feel. On squeezing these, a quantity of reddish brown serum, mixed with air, exudes. If this exudation is examined under the microscope (× 300) it is found to consist of granules of golden brown pigment; of large flattened cells, in which are numerous similar granules; and lastly, of coloured blood corpuscles in various styles of degeneration. Examine now the interlobular septa, and note that they are deeply pigmented, and frequently stand out very prominently. The deep layer of the pleura is similarly deeply pigmented, as are also the bronchial glands, which, in addition, are often enlarged and indurated. The wedge-shaped masses met with at the free margins are found to be solid (they sink in water). They are sharply defined from the surrounding tissues, and are of a deep plum colour, sometimes with a tinge of brown. If a scraping is taken from this surface it will be found to be made up principally of blood corpuscles, with here and there a few granules of the golden brown pigment. On the surface the large branches of the pulmonary vessels stand out more prominently, and therefore appear to be more numerous than in the normal condition. (See Nutmeg Liver, § 116, p. 94).

The bronchi must now be examined. Their inner surface is

usually deeply congested, and the mucous membrane is folded and corrugated looking; it has a watery or œdematous appearance, which is very characteristic of this condition. Harden a piece of the lung in which the brown induration is well marked, in Müller's fluid (§ 53, p. 42), another piece—with the wedge-shaped pulmonary apoplexy, some of the pleura, and a small bronchus—also in Müller's fluid, cut sections (§ 67, p. 48), and mount unstained in Farrant's solution.

Under a low power (× 50) the pleura appears to be enormously thickened, especially in its deeper layer, which is also deeply pigmented. Some of the pigment is black, other parts golden brown. The interlobular septa are in a similar condition, as are also the perivascular and peribronchial tissues. In the solid wedge-shaped mass the air vesicles have their walls thickened, and contain pigment, but this is partially masked by the enormous number of red blood corpuscles which fill the alveolar cavities. On the pleural surface there may be slight inflammatory changes, but these are by no means constantly met with.

In the portions in which the brown induration is well marked, the changes are very characteristic. The walls of the air vesicles are evidently thickened, and they have a peculiar beaded or varicose appearance. Along their lines pigment may be discerned, whilst in the beads (or loops, as they will afterwards prove to be) there is a greenish granular material, which may be recognised as composed of coloured blood corpuscles. Within the air vesicles similar small green granules may be observed, and also a number of large flattened cells, many of which contain a large quantity of pigment similar to that previously described. Most of these cells are lying free in the alveolar cavity, but others are attached to the beaded looking wall.

In a section stained with picro-carmine (§ 73, p. 53) the wall is stained pink, and all the fibrous bands are thickened.

In the wall of a bronchus the small blood-vessels are enormously distended, and can be readily distinguished even with this power. There is evidently an increased amount of fibrous tissue, and in the picro-carmine stained specimen the pink tissue is very prominent. The mucous membrane is thrown into folds, apparently by the tor-

tuous blood-vessels, which come very near the surface, and may even, in a small bronchus, rupture into the lumen. As a rule, there is but little of the bronchial epithelium left, as it is detached almost as rapidly as it is formed, by the serum exuded from the distended blood-vessels.

Under the high power (× 300), examine first the air vesicles, as it is in these that the most prominent changes are observed. Within the air vesicle are numerous flattened cells lying free. A few of these flattened cells may also be seen in section as nucleated spindle-shaped cells, closely applied to the wall of the air vesicle; but these are comparatively few in number. In most of these the golden brown pigment stands out very prominently. Along with the large cells are a

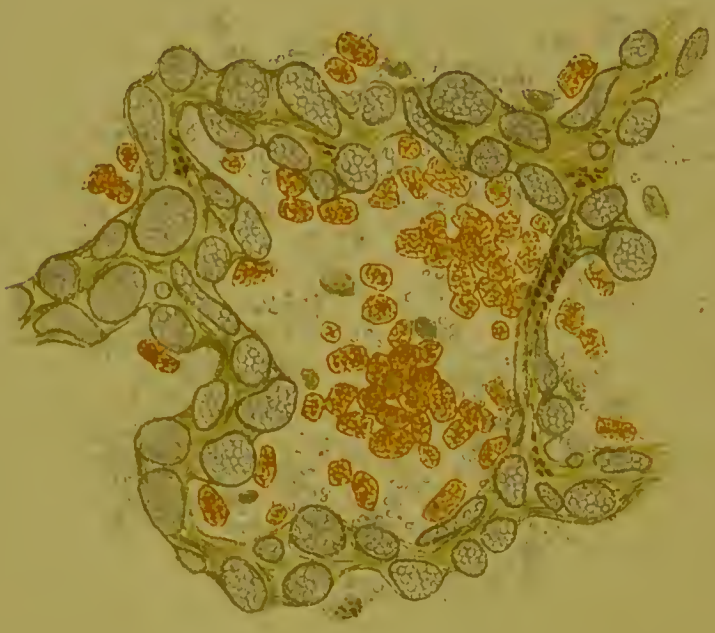


FIG. 65.—Drawing from section of brown induration of the lung. Unstained. (× 300.)

c.d. Distended capillaries of interalveolar septa.
c.b.c. Coloured blood corpuscles lying free in the air vesicle.
e.c. Epithelial cell detached.
ep.c. Epithelial or catarrhal cell containing large quantity of altered blood pigment.
p. Pigment taken into lymphatics of interalveolar septum.

At the point from which this was taken the pigmentation was very well marked, and the varicosity of the vessels is here also well seen.

few coloured blood corpuscles. Lying beneath the scattered epithelial cells are the capillary vessels of the wall; they are extremely

distended and varicose, and appear as loops or sections of vessels projecting into the air cavity. They were long mistaken for epithelial cells, and are still figured as such in many of the text-books; but by the aid of picro-carmine staining, the coloured blood corpuscles lying in the lumen of the vessel may be demonstrated as greenish coloured corpuscles, each of which has a double outline. These vessels also have a double outline, and in some cases there appears to be enormous thickening of their walls, a condition which has already been described in nutmeg liver (§ 116, p. 95). In the wall of the vesicle—that is, along the course of the lymphatics—there is a considerable deposition of pigment, of much deeper colour than in the cells, but still golden brown. A small proportion of it is black, and is simply carbon pigment derived from without. The pigment under this power is seen to be lying in the lymph spaces, free or enclosed, in cells, either epithelial from the air vesicles, or endothelial or connective tissue corpuscles.

Similar masses are met with in the interlobular septa and in the deep layer of the pleura, to both of which they have been transported from the air vesicles along the lines of the lymphatics. The peribronchial and perivascular lymphatics are also filled with pigment. In all these situations there is an increase in the amount of fibro-cellular tissue, an increase which is brought out very decidedly in the picro-carmine stained specimen; but after the pigmentation the enormous distention of the vessels is the most marked change, and it is to this dilatation especially that the thickening of the pleura and the increase in volume of the lung are due.

Examine the walls of the smaller bronchi in this section, and note how complete is the congestion of the bronchial mucous membrane. The vessels here, as in the walls of the alveoli, are distended, lengthened, and their walls thickened. At certain points they are so much dilated that they form a cavernous structure, almost like that seen in the centre of a lobule in advanced nutmeg liver. The other coats, especially the muscular coat, is usually somewhat atrophied by distension and pressure. The basement membrane is swollen and œdematous looking, and the few cells covering it are flattened, columnar or cubical. It will be observed that the most marked vascular changes take place around the bronchi, and beneath the

pleura towards the base of the lung, but that they are by no means confined to these situations. In the naked eye examination it was observed that there was dilatation and prominence of the vessels of the lung. This is evidently partly due to distention, but also partly to the same cause as it was in the granular contracted kidney, *i.e.*, thickening of the tunica intima, which in this condition is tolerably well marked.

The pulmonary apoplexies are to be further examined under the high power, and it may be noticed that they frequently coincide with the distribution of the bronchus; and the bronchus, as well as the terminal air cavities, is in such cases filled with blood. It must be remembered that hæmorrhages are usually met with only where the brown induration is due to valvular disease of the heart, especially of the mitral valve. Brown induration of the lung is simply a secondary condition induced by a primary disease of the heart. It first appears as a chronic venous congestion, in which there is an exudation of serum from the capillaries; this causes separation of a considerable part of the epithelium in both air vesicles and bronchi. At the same time blood corpuscles escape into the alveoli, and are taken up by the altered epithelium; these are further taken into the lymphatic system of the interalveolar septa, from which the pigment is distributed to all the positions mentioned, including the bronchial glands. At the same time the vessels become more distended, more tortuous and thickened, and so the condition of brown induration is gradually developed. A small portion of the pigment is carbon pigment; but by treating a pigmented section with a solution of ferrocyanide of potassium, and then with a dilute solution of hydrochloric acid, a blue reaction is obtained, even with some of the perfectly black pigment, which points to the fact that it is derived from blood pigment.

Between this brown induration and a rapid venous congestion there are many intermediate stages. The rapid venous congestion is characterised by the water-logged condition of the lung, the lymphatics being unable to carry off the fluid as it is exuded. On making a section into such a lung there is usually marked congestion, whilst from the cut surface there exudes an enormous quantity of frothy, watery fluid. The air vesicles are filled very rapidly with fluid, and the surface appears to be congested. On examination

under the microscope the epithelium is found to be detached, and usually to be lying free in the alveolar cavity, and the vessels to be distended with blood.

Fat Embolism of the Lung.

199. As usually described, there are few naked eye changes in the lung in this condition, but there are marked congestion and redness where the condition is met with in cases of death following diabetic

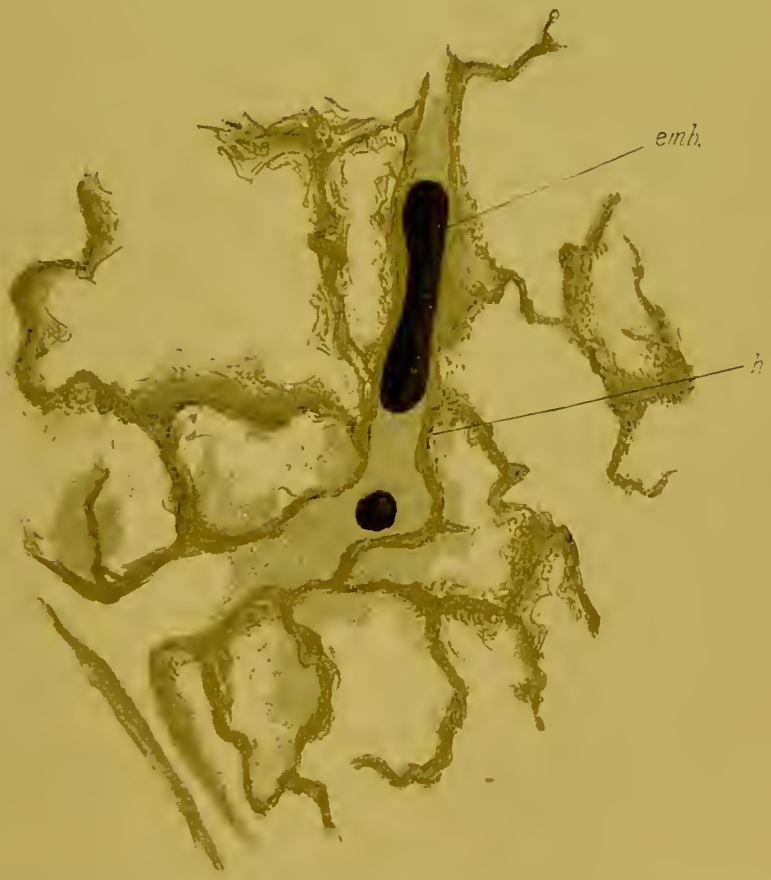


Fig. 66.—Fat embolism of the lung. Stained with osmic acid. (× 100.)

emb. Fat embolus stained black, filling one of the larger vessels.

h. Mass of coloured blood corpuscles in an air vesicle, the result of rupture of some of the smaller blood-vessels behind the embolus.

coma, or some œdema where the embolism follows fracture of a bone, especially of one of the cranial bones.

In the case from which this description was taken, and which was diagnosed during life as a case of fat embolism, due to fracture of

one of the cranial bones, there was deep congestion of both lungs, accompanied by a number of bright subpleural ecchymotic patches. These hæmorrhages were small, but they were very distinctly seen. On examination of a fresh section (§ 34, p. 31) bright refractile globules were observed in a number of the capillary vessels, and also in some of the larger branches of the pulmonary artery. These were stained black with osmic acid. In the stained specimen some of the emboli in the larger vessels were distinctly seen as elongated masses, completely filling the vessel, and ending at the point of bifurcation of the vessel. At the proximal end of the fat embolus the vessel had frequently ruptured, and there was an extravasation of blood into the surrounding air versicles. It was observed, too, that most of the emboli and most of the hæmorrhages were situated near the surface of the lung. This was to be expected from the distribution of the blood-vessels, as the terminal branches of these are always situated near the surface.

Harden a piece of this lung in methylated spirit (§ 52, p. 42), cut sections (§ 67, p. 48), stain one in osmic acid (§ 80, p. 62), and mount in Farrant's solution (§ 98, p. 71). Make a more careful examination, confirm the above points, and observe the different sizes and positions of the fatty globules. Some are extremely small, and are in the centre of the blood mass. Others are larger, and adherent to the wall of the vessel; whilst others again fill completely the lumina of vessels of very various diameters. Here, of course, the fat is stained black by osmic acid.

Similar hæmorrhages to the above are met with in cases of phosphorus poisoning, in septic fevers, anthrax, &c., and frequently in cases of active hyperæmia.

Disseminated Miliary Tuberculosis.

200. This is met with in the smaller form in acute general tuberculosis, especially in children. On examining a lung in this disease it is usually deeply congested, whilst between the congested patches are a number of pearly translucent or gelatinous-looking masses about the size of small-shot. These masses are much paler than the surrounding tissue, hence they stand out very distinctly. Over them there

is no pleurisy, but this is not invariably the case. At first sight the nodules appear to be scattered indiscriminately over the surface of the lung, but on more careful examination it will be found that they are situated in the lines of the interlobular septa, especially at the points of junction of the septa. Make a section into the lung, and note that the shot-like masses are found in the deeper layer of the pleura, at the point where the septa run into it. In addition, over the surface of the section, are similar masses, many of which are found along the lines of the larger septa, though some are seen in the lobule itself. The cut surface of the lung is deeply congested, and has a bright scarlet colour. The small shot-like bodies are scattered over the whole of the lung, but are usually more numerous in one lung than in the other, and also affect one lobe more than the other. A few of the nodules may be grouped together, in which case there is a mass, known as racemose tubercle. Put a piece of this lung to harden in absolute alcohol (§ 51, p. 42), a second in Müller's fluid (§ 53, p. 42), cut sections (§ 67, p. 48). Take one of the absolute alcohol sections, wash it well in distilled water, and transfer to Weigert's solution of gentian violet (§ 82, p. 63), and gently warm in a test tube. When warmed the section will be sufficiently stained in half an hour, otherwise it must be left for twenty-four hours. When the section is sufficiently stained, transfer to distilled water and wash thoroughly, afterwards to a twenty-five per cent. solution of nitric acid, where it must be left until the colour has disappeared (about half a minute). Further, wash in distilled water, after which stain for ten minutes with Bismarck brown (§ 87, p. 65), wash with absolute alcohol, place for a second or two in oil of cloves, and immediately transfer to turpentine—(the preliminary immersion in clove oil prevents the curling up and sticking of the specimen)—after which the section is mounted in Canada balsam, dissolved in benzole and turpentine (§ 100, p. 73).[1]

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[1] In place of gentian violet and Bismarek brown other colours may be used :—Ehrlich's fluid (§ 86, p. 65), along with methylene blue (§ 89, p. 66), Gibbes's magenta (§ 83, p. 64), with methylene blue or chrysoidin (§ 88, p. 67), Ransome's fluid (§ 84, p. 65), with methylene blue. There are numerous other methods of staining, to some of which reference will again be made ; but the best results are usually obtained with gentian violet and Bismarek brown.

Stain a section of the lung, hardened in Müller's fluid, with picro-carmine (§ 73, p. 53), and mount it in Farrant's solution (§ 98, p. 71). Examine one of the sections first for the structure of the tubercle masses. These may be composed of a single "follicle," or of several. Examine one under a low power (× 50), and note that it is growing in the interlobular septum, or in some cases from an interalveolar septum. In all essential points the mass resembles the tubercular mass in the liver. In the centre is a more or less fully formed giant cell, containing a large number of nuclei, which are usually arranged at the margin of the cell as a crimson ring, the centre appearing yellow (with picro-carmine). In some cases, in place of the giant cell in the centre, there may be a mass of caseous tissue, which has a granular appearance even under the low power, and is stained yellow. Around the giant cell is an open reticular tissue, the meshes of which are somewhat elongated and are concentrically arranged. In the elongated space there are but few small round cells, but there are numerous endothelioid cells, somewhat irregular in shape, many of them containing two or more nuclei. Passing now towards the periphery of this mass, numerous small round cells are found, which appear to be arranged in rows, these rows enclosing spaces. The spaces appear to be contracted alveoli, of which the rows of round cells form the thickened walls. Projecting into the air vesicle from the thickened wall are similar masses of endothelioid cells, pushing before them the epithelial layer. In the immediate neighbourhood of the solid mass the thickening of the alveolar walls is proceeding, and the cavities are smaller and appear collapsed.

Examine an artery and a bronchus, and notice that in some cases round cell infiltration is commencing; but in the section from which this description is taken there is no further evidence of tubercular affection.

Examine under the high power (× 300), and first observe a giant cell. It is a branching cell of considerable size, twenty or even thirty times as large as the small round cells. The centre is usually composed of a homogeneous substance, which with picro-carmine is stained a bright yellow. The processes which run from the cell appear to be continuous with those of the surrounding reticular tissue. The arrangement of the nuclei differs in different cases. In some giant

cells the whole of the nuclei are placed at the periphery of the cell, and where a section is made through the cell, these are all that can be distinguished; but where the upper half of the cell is above the section, a number of nuclei may be observed in the centre, whilst on focussing down, those at the periphery come into view. The nuclei are rounded or elongated, and the intranuclear plexus is very distinctly seen. Around the giant cell the endothelioid cells are numerous; they are very irregular in shape and size, some containing but one nucleus, whilst others have as many as four. The reticulum is very readily distinguished under this power, with the open spaces, and a few round cells lying within them, along with the larger cells. Towards the periphery of the mass the appearances are very distinctive. The small spaces (larger than the meshes of the reticulum) are collapsed air vesicles, bounded by the greatly thickened alveolar walls, in which there is evidently active connective tissue proliferation. The masses of large endothelioid cells are, however, much more distinctly pushing their way into the cavity, forcing before them the epithelial lining. The cells of which the lining is composed are in a condition very similar to that met with in interstitial pneumonia. They are cubical, and in some cases are of very great size (§ 196, p. 273). In the immediate neighbourhood of the tubercle nodule the interalveolar septa are considerably thickened, and the epithelial changes are commencing; the air vesicles appear to be collapsed, but there are no marked catarrhal or croupous inflammatory changes. In the centre of the tubercle mass, especially if it is composed of several tubercle follicles or giant cell systems, as is usually the case, there is often caseation, a process which here is similar to that met with in caseation of gummata. The tubercular masses are purely extravascular, as may be proved by injecting such a lung, and as fresh tubercle follicles are formed around the primary giant cell system, the central one is cut off from its nutritive supply, and it undergoes the caseous degeneration. In some cases this caseation comes on before the formation of a giant cell has taken place, or immediately after the growth of the large endothelioid cells: this is especially the case where the disease is very acute, in which case there may be a condition almost like that to be described as broncho-pneumonic phthisis. In the specially stained specimen now look for the tubercle bacilli,

which may be seen as violet-stained rods lying in the lymph spaces. Some of them may be in the giant cell, but they are best seen as they lie in the meshes of the network surrounding the giant cell. (For appearance of these bacilli see Fig. 70, p. 298).

The larger masses of tubercle will be best described under the head of chronic phthisis, in the production of which condition they play a very prominent part.

Caseous Broncho-Pneumonic Tubercle.

201. This has up to the present been a subject concerning which discussion has waged fast and furious, and even now there are numerous opinions as to the nature of the process. It will be well, therefore, to leave out from the description any theoretical or controversial statements, and to confine what is said to a pure description of the appearances which may be met with.

This condition is found in children as a form of acute tuberculosis. But in this form the tuberculosis appears to be specially confined to the lung, or, at any rate, it appears to be more advanced in this position than in any other organ in the body. It is essentially a tuberculosis of the lung, having an acute specific origin.

The lung is congested, with here and there patches of collapse; whilst standing out prominently from the congested surface, either through the pleura or from the cut section, are a number of small nodules, one-twelfth to one-sixth of an inch in diameter. They are most numerous at the apices and towards the roots of the lung. These masses may be rounded or irregular in outline, some of them appearing to be branched and elongated. Each mass has a typical appearance; towards the periphery the tissue is firm, greyish, and gelatinous, whilst the centre is soft, pale yellow, and granular in appearance.

On squeezing the section a quantity of tenacious, muco-purulent material is pressed out from the various sized bronchi, especially from the smaller ones.

Harden a piece of this lung in absolute alcohol (§ 51, p. 42), and a second in Müller's fluid (§ 53, p. 42), stain and mount sections as for tubercle (§ 200, p. 283).

Examine under a low power (× 50 or × 20), and notice that each patch of the solidified tissue has a similar arrangement, the details differing only according to the direction in which the section is made through a bronchus, with its dependent air vesicles. If a transverse section of a terminal bronchiole be obtained, the following features may be observed :—Towards the centre, or a little to one side of the mass, is a rounded opening, or what was an opening, plugged up with a mass of small rounded catarrhal or purulent looking cells. These, of course, appear under this power to be granules simply. In the centre of the mass is a quantity of more or less homogeneous material, which, with picro-carmine, takes on a yellow stain ; and in this yellow material the outlines of the individual air vesicles can seldom be distinguished, though in some few cases they can be discerned. Around the caseous centre there is a zone of air vesicles in which there is no caseation, but in which there are distinctly marked changes.

In all the vesicles of this zone there are evidences of catarrhal (§ 191, p. 258) or croupous (§ 181, p. 233) pneumonic deposits, the interalveolar septa are thickened, and stand out somewhat prominently. Around the bronchi there is also an amount of thickening, due apparently to peribronchitis, similar to that met with in catarrhal pneumonia (§ 191, p. 258). In this form the fully developed giant cell tubercle is comparatively rare, caseation taking place before the organisation of the follicle has reached such a stage. The changes can best be observed where the process is commencing, or just at the margins of the caseous mass.

Under the high power (× 300) examine the small air channel, and note that it is filled with cellular elements, which very closely resemble the catarrhal cells already examined. In this mass of cells in the specimen stained with gentian violet and Bismarck brown are numerous rod-shaped tubercle bacilli. In the centre of the acinus, where the caseation is most advanced, a mass of granular *débris*, stained yellow, may be observed. Near the margin the interalveolar septa may also come into view. Tubercle bacilli are found in this position, and in some cases they are exceedingly numerous. At the margin of the caseating mass the epithelial cells are undergoing other changes than simple catarrh ; they appear to be arranged in columnar processes

—(this is especially well seen in a fresh specimen, cut and stained in picro-carmine)—extending into the alveolus for some little distance. The cells of which these columns are composed have a peculiar hyaline appearance; they are stained yellow with the picric acid of picro-carmine, but they very rapidly become caseous. In those cells which are the result of a true catarrhal process, there is frequently an œdematous condition or a simple fatty degeneration—changes which are quite distinct from the caseous condition.

Examine, too, the fibrous septa near the caseous centre, and note that in these and in the interalveolar septa there is a great amount of small cell infiltration; and in these, as nutrition is cut off by the

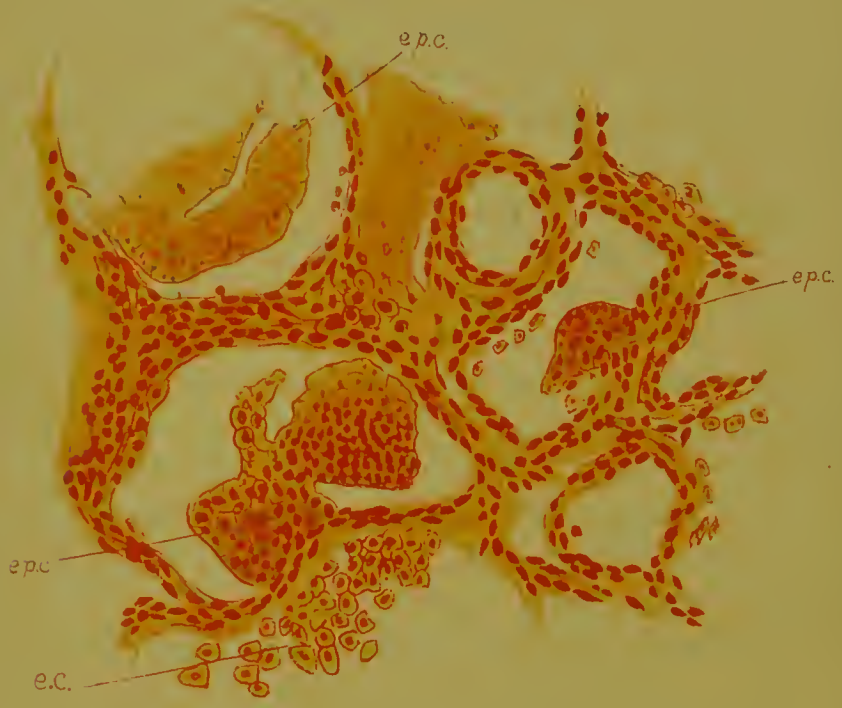


FIG. 67.—Section of lung. Acute tuberculosis. Stained with picro-carmine. (× 300.)

e.c. Growth of large endothelioid cells.

ep.c. Growth of epithelial cells into alveolus. These cells are arranged somewhat in columns, and are undergoing rapid caseation. Mass is yellow and homogeneous at surface.

Between the air vesicles the septa are somewhat thickened, and some of the air vesicles are apparently diminished in size by the encroaching epithelium.

occlusion of the vessels, the caseous metamorphosis also occurs. In very thin sections tubercle bacilli may be distinguished not only in

the lymph spaces in the thickened interalveolar septa, but also in the epithelial cells which line the air vesicles, at the point where the columnar proliferation is taking place.

It will be noted here that the air cavities in connection with the terminal bronchioles are the areas in which the changes are observed; and if a vertical section be made through the bronchiole with its terminal cavities, the caseous mass is always situated near the bronchiole, and the pneumonic zone is nearer the periphery.

Closely allied with this condition is a form of acute phthisis, often spoken of as broncho-pneumonic phthisis, though it must be remembered that all cases of acute phthisis are by no means due to this broncho-pneumonic or caseating catarrhal condition.

Acute Phthisis.

202. Acute, rapid phthisis is a condition in which there appears to be a process almost like broncho-pneumonic tubercle, associated with more extensive changes. On examining a lung from such a case, the pleura is, as a rule, somewhat thickened, especially over the apex, though this may not be very marked. The whole of the lung is solid, and beneath the pleura large pale yellow patches are seen, radiating from which are numerous similar bands. On section into the lung there is usually evidence of more chronic process at the apex. There may be a cavity of considerable size, the walls of which are firm and indurated and may be pigmented; over this cavity the pleura may be considerably thickened. Around the cavity the changes are more acute, but the appearances are evidently considerably modified by the presence of the more chronic changes. In the lower part of the lung, however, the changes are more prominent and characteristic.

The lung is solid. Scattered over its surface are the large, rounded, pale yellow patches, from which processes run out in same manner as under the pleura. Between the yellow patches—which in shape may be compared to bunches of grapes, of which the bronchioles form the stalks—are bright red lines, in which the caseous process has not as yet become marked. Towards the base the yellow patches are so large and so numerous that they run together, and obscure every other change.

Squeeze the section, and note that there exudes a thick, tenacious, muco-purulent material from the bronchi; the walls of the bronchi are thickened and appear extremely gelatinous; the bronchial glands may be swollen, œdematous, or softened and caseous.

There may be all stages between this and the form which will be next described. The yellow patches, and even the appearances of a great part of the lung, may be similar to those met with in broncho-pneumonic tuberculosis, except that the destructive processes are more pronounced; or there may be patches of grey granulations, wedge-shaped near the surface, racemose, or in clumps in the substance of the lung, all of which are surrounded by pneumonic patches, and are in various stages of caseation, and are more chronic than the form first described; the microscopic changes vary considerably, but will be readily traced out if such sections are compared with the various conditions here described. Harden pieces of the different parts of the lung in absolute alcohol (§ 57, p. 42); others in Müller's fluid (§ 53, p. 42), cut sections (§ 67, p. 48), stain one in picro-carmine (§ 73, p. 53), and mount in Farrant's solution (§ 98, p. 71); prepare another for bacilli (§ 200, p. 283).

Examine one of the pale yellow patches under a low power (× 50), and note that it is made up of a series of centres, each of which has a special and distinctive arrangement. Each has a caseous centre, in which the walls of the alveoli are involved, as well as their contents. At this point there are no vessels. Further from the centre is a zone, in which the alveolar walls are somewhat thickened, and in which the blood-vessels are not very readily seen. There is considerable catarrh in this position, parts of the products being stained black if a section be treated with osmic acid. Still further away are early catarrhal or croupous pneumonic patches, either of which may be readily recognised, and in this region the capillary vessels are usually considerably distended. These areas have frequently become fused by the extension of the pneumonic process, and it is in such cases that great destruction of tissue occurs. Examine the pleura, and observe that it is thickened and extremely vascular, with a considerable number of granulation loops passing to the surface, and that at points the two pleural surfaces have become joined together. Examine part of the lung tissue near the apex, and note that here there are

usually evidences of a chronic interstitial pneumonia, with chronic tubercle, to be afterwards described; whilst around the parts thus affected the tissues may be in an advanced state of caseation, and smaller cavities are formed by the breaking down and evacuation of the caseous material. The vessels around these patches, as in interstitial pneumonia, &c. (§ 196, p. 272), are in an advanced stage of endarteritis obliterans.

Around the bronchi are found changes similar to those met with in broncho-pneumonia, or even tubercle nodules in an early stage of development.

Confirm these appearances under the high power (× 300). The course of the disease is apparently very rapid, but the rapidity varies in different cases. If the patches are more or less separated, and the caseous changes are taking place only at intervals, the course of the disease is comparatively slow, and the appearances, both naked eye and microscopic, closely resemble those found in broncho-pneumonic tubercle; but when the masses rapidly run together, owing to the rapidity of the catarrhal and croupous pneumonic changes and the formation of cavities of considerable size, the course of the disease is usually extremely rapid. In whichever form the disease is met with, tubercle bacilli are found in large numbers, especially at the points where the proliferation of epithelial cells is greatest, and where the connective tissue corpuscles are also undergoing rapid proliferation. Where the caseation is advanced the bacilli are not so readily distinguished. To find them, it is necessary to use a somewhat higher power (× 600) than that used in the examination of sputum.

Common Chronic Phthisis.

203. This is a form of lung disease which may run a very slow course, in which the symptoms during life are very well marked, and in which the pathological changes are extremely characteristic.

On opening the chest it will be noted that the lungs are firmly adherent to the surrounding tissues, especially at their apices (if the disease occurs on both sides), though frequently one lung only is affected. The adhesions may be so extensive that the pleural cavity is almost obliterated, especially at its upper part. The pleuræ are

much thickened, and are fibrous looking, and on examination of the surface of the visceral layer, bluish grey gelatinous nodules may be observed. On palpation the surface of the lung feels hard, firm, and fibrous, but somewhat irregular, whilst lower down are a number of hard wedge-shaped or nodular masses at the margins or in the substance of the lungs.

Make a section through the lung, and note approximately the following appearances. At the apex the thickening of the pleura is extreme, as much as a quarter of an inch, or even more in some cases. Under the thickened pleura, and usually very near the apex, are cavities, one or more in number, each of which is bounded by firm fibrous walls, with a glistening lining, and usually containing a soft caseous looking mass, which partially fills the cavity. These cavities vary very greatly in size, "from that of a hazel nut up to that of a small orange." The fibrous wall of the cavity is deeply pigmented, and appears to be continuous with the thickened pleura. Throughout the whole lobe are bands of fibrous tissue, most numerous around the above-mentioned cavities, but also following the lines of the interlobular septa, the deep layer of the pleura, and the peribronchial and perivascular tissues. In the fibrous tissue small yellow caseous looking masses, similar to those seen in stone-masons' phthisis (§ 195, p. 267), are met with, and they appear to be formed in the same manner as in that condition. Now examine the wedge-shaped masses described as occurring in the lung under the pleura. They are in the form of bunches of grapes, the base of the pyramidal mass being situated towards the pleura. From the apex, the stalk, consisting of a line of small round nodules, is seen to extend. In the substance of the lung rounded masses of similar appearance are met with, packed closely together in the upper part of the lung, but with large highly vascular areas of lung tissue between them towards the base. These larger masses are composed of small rounded or ovoid shot-like bodies, hard and firm to the touch, and of a bluish grey colour, the centre frequently being very fibrous, and deeply pigmented, and the peripheral zone frequently gelatinous and even pink. In some cases the centre, in place of being hard and fibroid, is somewhat softened, and may be slightly yellow, but where this is the case the growth appears to have been somewhat

more rapid than in the above form. Around the bronchi similar masses are seen. These are the so-called tubercle masses, but it must be borne in mind that each of these is not a simple body, but is made up of several tubercle follicles. Around the larger areas are a number of smaller areas, which are usually surrounded by a pneumonic zone. These changes are always most marked in the upper lobe of the lung, where the masses may have become so fused that they present a solid area, in which, however, there are caseous or calcareous masses, due to degenerative changes, in which case the tissues of which the solidified parts are composed are very fibrous and deeply pigmented. In the lower lobe the several tubercle masses are more distinct, have not undergone fibroid or caseous changes, and have between them lung tissue more or less congested.

In some few cases the base of the lung is in an advanced stage of the so-called acute phthisis. The lower lobe is solidified, yellow, caseous, and exactly in the condition described as that of acute phthisis (§ 202, p. 289). This appears to be quite a secondary condition, and usually occurs in one lung only.

Harden pieces of the lung from various positions in absolute alcohol (§ 51, p. 42), or in Müller's fluid (§ 53, p. 42), cut sections (§ 67, p. 48), and stain and mount as for preceding sections (§ 200, p. 283).

Examine under low powers (× 20 and × 50). Each nodule is composed of a number of giant cell systems or tubercle follicles, each of which has the structure previously described (§ 123, p. 115), the oldest follicles being near the centre, the youngest at the periphery.

In the extremely chronic condition the giant cell systems are most perfectly developed at the periphery of the nodule, whilst the central part is caseous, or, more frequently, the centre has become quite fibroid, whilst the peripheral fibrous network has become compressed, and then forms a mass of dense fibrous tissue. The younger tubercle follicles around the primary follicle are readily distinguished by their more typical structure. Under this power observe the positions in which the nodules occur. In the deep layer of the pleura they are numerous, also in the interlobular and interalveolar septa and the peribronchial and perivascular tissues, all of which are greatly thickened. It is a significant fact, as often pointed out,

that the tubercle nodules follow very much the same course as the pigmented nodules and pigment injection in anthracosis, &c., *i.e.*, the course of the lymphatics. Note, too, that the tubercle follicles are growing into the air vesicles from the interalveolar septa. These may be seen in various stages of development. One may be represented by thickening of the septum only, where a number of small round cells and some large endothelioid plates are seen occupying the space around the capillary vessel. At other points the cellular mass appears to be projecting into the alveolus, pushing the epithelial lining of the air vesicle before it. Usually a giant cell is to be observed in the centre of such a follicle, the centre stained bright yellow, the nuclei at the periphery crimson. Around the tubercular nodules are numerous patches of catarrhal or croupous exudation. There may be an actual

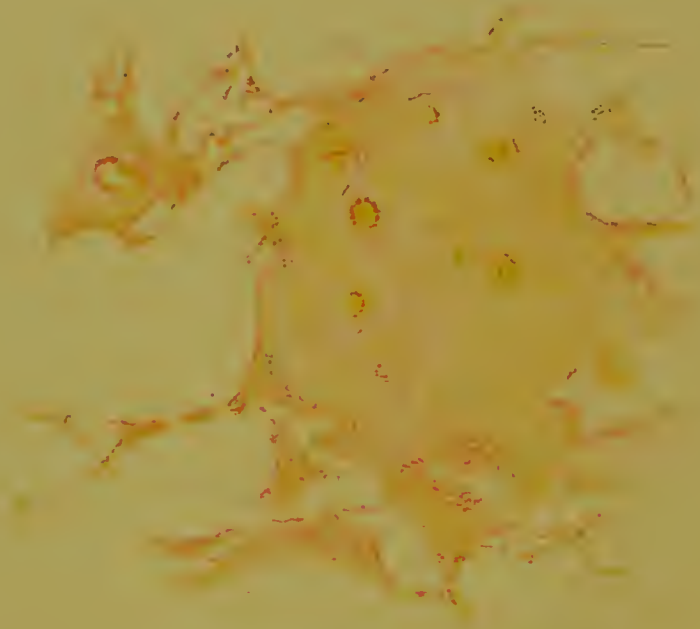


FIG. 68.—Section of chronic tubercle of the lung stained with picro-carmine. (× 50.)

g.c. Giant cells in centre of tubercle follicles, yellow homogeneous centre of cell, with deep crimson ring of nuclei.
The whole group of follicles forms a tubercle nodule, surrounded by comparatively healthy lung tissue (*l*).

tubercular growth in the walls of the bronchus, extending into the lumen and diminishing its size, and even ulcerating on the mucous surface; a similar condition on the walls of the vessel leading to partial obstruction of its lumen. In addition to these changes in the

wall of the vessel, there is frequently endarteritis obliterans. The croupous form of pneumonia is much more commonly met with than the catarrhal.

Under a high power (× 300) examine the deep layer of the pleura, and observe the tubercular and fibroid masses, also similar masses in the interlobular and interalveolar septa and in the peribronchial and perivascular tissue. In the wedge-shaped patches near the surface the tubercle nodules, surrounded by pneumonic zones, should be further examined; and these patches may be taken as typical of those in the whole of the lung, with the exception of those at the apex, where the fibroid changes are most marked.

Each patch is made up of tubercle nodules, which again are composed of tubercle follicles. In the centre of the nodule the tissue is

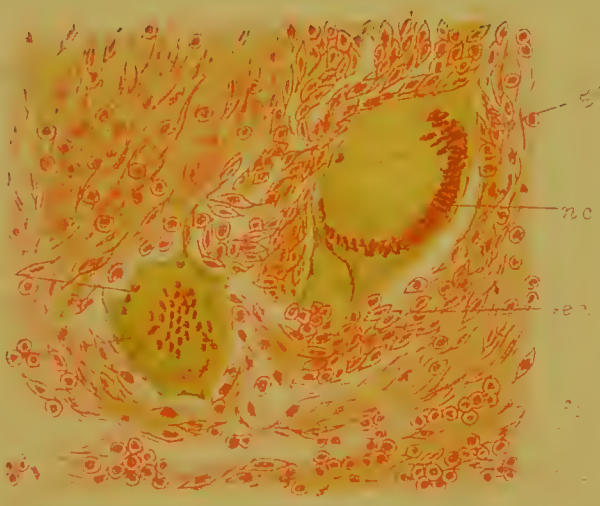


FIG. 69.—Giant cells from case of chronic tuberculosis of the lung. Stained with picro-carmine. (× 300.)

g.c. Branching giant cells with yellow homogeneous basis.
n.c. Nuclei of giant cell.
e.c. Endothelioid cells lying on delicate network around giant cell.
f.t. Fibrous stroma, here more fully formed, comparatively few endothelioid cells near the periphery, but a considerable number of smaller and rounded (*e.t.c.*) cells are seen. These are simply such cells as are seen in rapidly proliferating connective tissue.

caseous and stained yellow; passing further outwards there may be seen masses of granular *débris*, in which are a few angular and shrivelled cells, with here and there fatty globules or granules, which are stained black by osmic acid. Around the central caseous mass,

which is simply caseous tubercle, is a zone of tubercle follicles, each of which has the regular giant cell structure. Further out again is a zone in which are tubercle follicles, growing principally into the air vesicles, and usually accompanied by pneumonic exudation into these air vesicles. Examine one or two of the tubercle follicles in the interalveolar septa, the endothelioid cells of various forms and sizes, and the small round cells, all formed by proliferation of the endothelium of the lymphatics, and of the proliferation of the connective tissue corpuscles. As this mass grows, it is seen to make its way into the alveolus, pushing before it a regular layer of epithelium. This afterwards desquamates, and the connective tissue grows further outwards, further formation takes place, the giant cell makes its appearance, and the full tubercle follicle is developed. Around the tubercular nodules there is, as seen above, an inflammatory exudation—croupous in the more chronic forms, catarrhal in the more acute. These have been already described (§ 181, p. 233, and § 191, p. 257), and it is not necessary to enter more fully into their appearances.

Tubercle bacilli are much more rare in this form than in the more acute process, but they may be found in the specially stained specimens (§ 200, p. 283), particularly during the earlier stages of tubercle formation. They must be looked for with a high power (× 600) in the lymph spaces, where the proliferation is taking place most rapidly.

In exceedingly chronic tubercle (fibroid) there may be no surrounding inflammatory changes, the giant cell becoming organised into connective tissue, and remaining quiescent.

The bronchial glands, on microscopic examination, are found to be tuberculous, pigmented, fibroid, or are frequently in a condition of caseation.

After the above description it will be understood that phthisis is a condition of the lungs in which destructive changes take place, first in the form of consolidation, tubercle formation, accompanied by the various forms of pneumonia, interstitial, croupous, and catarrhal, with obliteration of the blood-vessels, and disturbance of the lymphatic circulation, leading to fibrous tissue formation, or to ulceration, as the case may be. The changes in the walls of the bronchi lead to weakening, or even to ulceration; the changes in the septa may lead to fibrous tissue formation, whilst similar changes or caseation may

result throughout the whole of the lung substance. Caseation and cavity formation are most frequent in the upper part of the lung, where, too, the process is, as a rule, more chronic, but more advanced. The various forms of cavity formation have been already described (§ 197, p. 274); and as there is really no specific method of cavity formation, the reader is referred to that description.

Before concluding this short description of the pathological condition of the lung, it will be necessary to say a few words as to the treatment of sputum (the contents of phthisical cavities, &c.), in order to demonstrate the presence of (*a*) the elastic membrane of the alveolar walls, which resist pathological processes far more than most of the tissues; and (*b*) tubercle bacilli. For the examination and significance of other structures, such as epithelium, and of other forms of bacilli, the student is referred to systematic treatises, and to other sections of this work.

To separate the elastic tissues Fenwick's method is undoubtedly the best. He boils the sputa in a beaker with caustic soda or potash, until all the mucin, &c. is dissolved. A quantity of water is then added to the fluid, and the whole is put aside in a conical glass. The elastic fibres are unaffected, and sink to the bottom of the glass, whence they may be removed by means of a pipette, transferred to a slide, and examined.

Tubercle Bacilli.

204. These are very readily found in sputum by the aid of the following methods. Baumgarten's method (*Lancet*, 15th July 1882).—Take a small quantity of sputum with a needle, and smear it on a cover glass, press another against it, and wipe away any which may appear at the edges with a bit of blotting-paper. Separate the cover glasses, when each will be found to be covered on one side with a thin film of sputum. Pass the glasses several times through the flame of a spirit lamp, after allowing the film to dry. By this means any albumen present is coagulated. The glasses are then immersed in a solution of a couple of drops of 33 per cent. solution of caustic potash added to a watch-glass full of distilled water. Press the cover glass down on a slide, and examine under a high power (× 600), when the bacilli may be distinguished as small rod-like bodies, about a

quarter to one-third the length of the diameter of a coloured blood corpuscle.

"In order to preclude the possibility of confounding the bacilli of tubercle with those of other species, the cover glass may be raised and placed aside until the layer of fluid on its under surface is dry, and then passed two or three times through a gas flame, and then on it may be placed a drop of ordinary watery solution of aniline violet, or any other nucleus tinting preparation of aniline. All the putrefactive bacteria then appear under the microscope as an intense blue or brown (according to the testing agent and its strength, while the tubercle bacilli remain absolutely colourless, and can be seen with the same distinctness as in the ordinary potash preparation. The whole process does not occupy more than ten minutes."

The bacilli in the sputum may also be stained by the same reagents as have already been described in connection with the staining of lung tissues.

The sputum is spread on the cover glass, and treated as above to fix the albumen. It is then allowed to stand in one of the staining



FIG. 70.—Tubercle bacilli in sputa, stained with gentian violet. Contrast stain Bismarck brown. Weigert's method. (× 450.)

fluids (floating face downwards) for from five minutes to half an hour, according to the strength and temperature of the fluid. It is now removed, washed in distilled water, transferred to a solution (1-4) of nitric acid, as the ordinary solution (1-2) usually proves too strong (though it is here not so important that the solution should be weak, as it is in the case of delicate sections, which are manipulated with

difficulty after being treated with the stronger fluid). Leave in this for about half a minute, and then transfer to distilled water, wash thoroughly, and use a contrast stain (§ 87, p. 65, *et seq.*), wash in absolute alcohol, clear up in turpentine, and mount in Canada balsam dissolved in benzole and turpentine (§ 100, p. 73).[1]

Other Pathological Conditions met with in the Lung.

205. Pyæmic abscess is sometimes met with in connection with a general condition of pyæmia. In such a case the abscesses are near the surface, and over the inflamed and degenerating tissue there is usually acute pleurisy. Similar small abscesses are sometimes met with where there has been pressure on a bronchus, by an aneurism for instance, leading first to pneumonia, pleurisy, and ultimately to small abscess formation. Examine the vessels in the deep layer of the pleura and near the abscess. They and the lymph spaces in the neighbourhood are distended, and in many cases masses of micrococci are met with in these positions.

In farcy there are frequently evidences of catarrhal pneumonia, fat embolism of the lung, &c., and small bacilli are described as present in the lung in this condition around both air vesicles and bronchi. Small abscesses are also met with in the lung in actino-mycosis, in or near which abscess the characteristic mycelial fungus is found.

Other Parasites met with in the Lung.

Hydatids, *Filaria bronchialis* (especially in sheep), and sometimes, but rarely, the *Cysticercus cellulosæ*.

Primary Tumours of the Lung.

206. *Lipoma* and *osteoma* are sometimes met with.

Rokitansky describes also *fibroma* of the lung.

Chondroma or *enchondroma*, growing in connection with the bronchial cartilages, occurs in the lung.

Cylindrical or *columnar celled epithelioma* appears in the lung as a primary growth in connection with the bronchial glands and ducts.

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[1] For Heneage Gibbes's method of double staining see foot-note, p. 64.

Squamous epitheliomas are also described as occurring in this position, but very rarely.

Secondary Tumours of Malignant Types.

207. These are very numerous in the lung. Of these, because of the extreme vascularity of the organ, the most common are the *sarcomas*, especially the more malignant forms. (See section on sarcoma).

The *melanotic sarcoma*, which appears as a somewhat flattened or rounded mass, especially immediately below the pleura, is deeply pigmented, and the structure is the same as when it occurs in any other position.

The same may be said of the other forms of sarcoma as regards structure, but these occur much more frequently in the substance of the lung, and not so frequently near the surface.

Lymphosarcoma, *lymphadenoma*, which usually spread from the mediastinum.

Small round-celled sarcoma, and *small spindle-celled sarcoma*, *osteo*, *osteoid*, and *myeloid sarcomas*.

Malignant enchondroma, secondary to the same condition in the testicle.

Myxochondroma, secondary to myxochondroma of the periosteum of the scapula (Greenfield). This is met with as semi-gelatinous bluish cartilaginous masses in the branches of the pulmonary artery, the branchings of which they closely follow.

Cancers—scirrhous, *encephaloid*, *colloid* and *adenoid* (or the columnar celled epithelioma), and *squamous epithelioma* (which is usually secondary to that of the tongue when it spreads through the mediastinal glands).

These forms of cancer may all occur in the lung, as there is a very free distribution of lymphatics and lymphatic glands in this organ and in its pleural covering. They are almost invariably multiple.

In this position it is somewhat difficult to distinguish them from the sarcomas, especially in the earlier or softer forms, but later and in the harder forms puckering of the pleura and umbilication frequently occur, as in scirrhous cancer of the breast. Microscopically they resemble the same tumours in other organs. (See section on Tumours.)

CHAPTER VIII.

THE SPLEEN.

Normal Histology.

208. The spleen is a flattened, somewhat crescent shaped organ, usually from five to five and a half inches in length, three or four inches across, and one to one and a half inches in thickness, though these measurements vary considerably in different cases. The weight is usually from five to seven ounces, though this also may vary considerably, as, "even when perfectly free from disease, it may fluctuate between four and ten ounces" (Quain's Anatomy). The anterior margin is notched, and it must be remembered that the notches persist, however large the organ may become. On the concave surface of the spleen is a vertical fissure, termed the hilum, at the bottom of which are numerous openings, where the blood-vessels enter or emerge.

Investing the organ is a serous coat, which is simply a reflection of the peritoneum over the spleen, forming its capsule. It is covered with a layer of flattened endothelial cells, which, seen in section, are spindle-shaped. Beneath this is a layer of connective tissue, in which are elastic fibrils. Beneath the last-named layer is a denser mass of connective tissue, in which are blood-vessels, nerves, and a few fibres of non-striped muscular tissue. Running in from the hilum on the one hand, and from the deeper layer of the capsule on the other, are numerous septa or trabeculæ, composed of connective tissue and of bands of non-striped muscular fibre, evidently continuous with that of the capsule. These trabeculæ divide and subdivide until the ramifications become very small, and the terminal filaments of the trabeculæ from the capsule meet those from the hilum, and thus form a supporting framework of connective tissue.

The arteries of the spleen enter at the hilum, and are first, together with the veins, carried along the trabeculæ, in which position there are numerous perivascular lymphatics. Soon the artery leaves the vein, and at once breaks up into a tuft or pencil of small arterioles. These leave the trabeculæ, and are continued into the splenic substance proper. After leaving the fibrous septum, each arteriole is invested with a mass of tissue known as an adenoid sheath. This

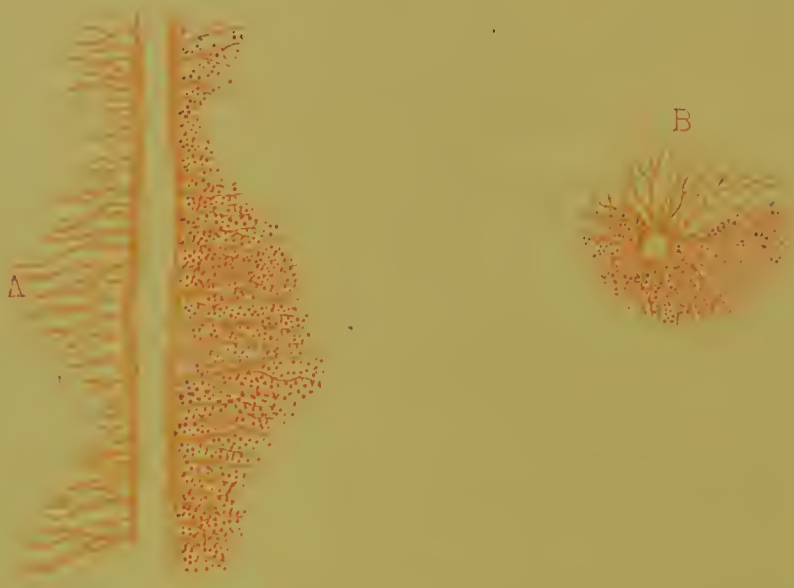


FIG. 71.—Diagram representing the arrangement of the capillary vessels in the adenoid sheath (Malpighian corpuscle).

A. Longitudinal section of the arteriole, with its sheath.
B. Transverse section.
a.a^1. The capillary vessels which convey the blood from the small arterioles to the splenic sinuses.
b.b^1. Adenoid tissue between these capillary vessels.

sheath is a moniliform mass, in which the artery is usually placed somewhat eccentrically. There are therefore enlargements, bulgings, and constrictions in this adenoid sheath. This is the so-called Malpighian corpuscle. It is composed of a reticular stroma, lying on the bands of which are endothelioid cells, whilst lying in the spaces are numerous small round corpuscles or lymphoid cells. This tissue is very dense, and even under the naked eye is usually readily seen, as are also the fibrous trabeculæ. Proceeding from the central artery are "elongated meshes of capillary blood-vessels," which run nearly at right angles to the long axis of the sheath, until they come to its margin, when they open out into the pulp tissue, first into a

series of small sinuses, and then into larger venous sinuses, after which the blood is collected into the venous trunks, and carried from

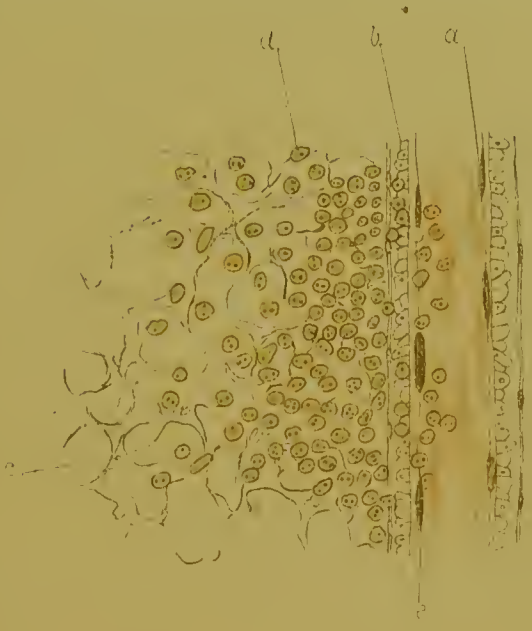


FIG. 72.—Part of a Malpighian corpuscle of the spleen of man. (× 350.) (After Klein and Noble Smith.)

a. Arterial branch seen in longitudinal section.
b. Adenoid tissue, consisting of adenoid reticulum, in which the nuclei of the lymph corpuscles may still be seen.
c. Reticular structure, from which the lymph corpuscles have been removed accidentally.
d. Muscular fibres of the middle coat of the vessel seen in transverse section.
e. One of the endothelial cells lining the vessel.

the organ along the trabeculæ to the hilum, and then to the portal vein.

The splenic pulp is the tissue between the adenoid sheaths or Malpighian corpuscles which is supported by the connective tissue network. It is composed of a mass of sponge-like structure, in which are small open spaces communicating with the capillary vessels as they emerge from the adenoid sheath. The spaces are bounded by large endothelial cells or plates lying on a trabecular tissue. These cells are transparent, and usually contain one or more large nuclei. In the sinuses are numerous lymphoid corpuscles, in which, as well as in the endothelial cells, blood corpuscles, or pigment derived from them, are found imbedded. There may be a few large cells partially attached to the epithelial cells by stalks or pedicles (the

cells proliferating by budding). Opening out from these smaller sinuses of the pulp are larger tubular sinuses, lined with similar endothelial cells, and containing large and small nucleated cells, and usually some coloured blood corpuscles. Supporting the walls of the larger sinuses are bands or fibrils of yellow elastic tissue, which are arranged almost like barrel hoops. From these larger or venous sinuses the blood is poured into the venous trunks.

Examine under a low power a section of a healthy spleen hardened in Müller's fluid (§ 53, p. 42), stained in picro-carmine (§ 73, p. 53), and mounted in Farrant's solution (§ 98, p. 71). Note the capsule with the trabeculæ running at right angles to it. Between the trabeculæ observe the rounded masses of denser looking tissue, which even under this power appear to be extremely cellular (lymphoid tissue). These denser masses, the Malpighian corpuscles, vary considerably in size and shape, according to the direction in which the section is made. They may be rounded if cut transversely, oval if cut obliquely, and elongated, and even bifurcated (at the point of bifurcation of a vessel), if the section passes vertically through the adenoid sheath. The size varies according as the section passes through an enlarged or a constricted part of the sheath. The vessel is situated at some distance from the centre, and may even be at the margin of the Malpighian corpuscle. Surrounding the Malpighian corpuscles the splenic pulp is recognised as a spongy open network, in which the sinuses vary in size, those nearest the Malpighian bodies being considerably smaller than those further away. Running through the splenic pulp, as will afterwards be better observed in the waxy spleen, are numerous small arterioles, which are apparently not in communication with the arterioles of the Malpighian bodies.

Under the high power (× 300), the various features above described must be observed, and special attention paid to the capillaries in the Malpighian bodies, the lymphoid tissue of which the Malpighian body is composed, the arterial sinuses, with their endothelial lining, the large round and nucleated cells, the smaller lymphoid cells, and the coloured blood corpuscles. Note, also, the similar structures in the large venous sinuses, and the encircling elastic bands in the walls of these sinuses. Under this power, too, observe the connective tissue and non-striped muscular fibre in the trabeculæ.

Active Hyperæmia of the Spleen.

209. In this condition the spleen undergoes changes which are very evident to the naked eye, but which, under the microscope, are not so characteristic.

Hyperæmia is met with in almost all cases where there has been high temperature continued for any length of time, but in its most acute form it is met with in septic, specific, and malarial fevers, and in syphilis. In this condition the organ is enlarged, in some cases to two or three times the normal size, the capsule is stretched, and the organ, when cut into, is soft, diffluent, and extremely vascular, and is of a dark red colour when the section is first made. This dark red rapidly turns to a bright arterial red when the tissue is exposed to the action of the air for a few minutes. In the more acute septic conditions, such as typhus or acute septicæmia, there is, as before stated, a more acute hyperæmia, and the tissue is bright red, or even pink, when the organ is first cut into, especially in the early stages of the disease; if the patient lives for a time, the tissue still remains soft, but it becomes paler and almost creamy, and the trabeculæ and Malpighian bodies cannot be easily distinguished in the mass of soft creamy looking pulp.

In the most acute form, *i.e.*, that met with in malarial fevers, the enlargement of the spleen may be so great and so rapid that the organ may rupture.

In smallpox, scarlet fever, and typhoid fever, the spleen may, instead of being diffluent, be considerably firmer than in the above forms, especially in the later stages of these diseases. Here the enlargement is very great, and the organ may reach as much as four times its ordinary size. The Malpighian bodies are considerably increased in size, owing to swelling of the adenoid tissue. The whole surface has a peculiar greyish, or sometimes yellowish, tinge mixed with the red.

This active hyperæmic stage may be followed by a stage of resolution, as in a spleen taken from a case of acute pneumonia, in which death supervened during the stage of grey hepatization or early resolution. In this case the organ was considerably less than even the normal spleen, the pulp appeared to be greatly diminished in

quantity, and the trabeculæ stood out very prominently as white fibrous bands passing in from a somewhat thickened and greatly wrinkled capsule. If it is intended to look for bacteria, the organ should be hardened in absolute alcohol (§ 51, p. 42); but if the examination is for structural changes, Müller's fluid alone (§ 53, p. 42), or Müller's fluid and spirit (§ 54, p. 43) should be used as the hardening reagent. Cut sections (§ 67, p. 48), stain one in picro-carmine (§ 73, p. 53), and mount in Farrant's solution (§ 98, p. 71): stain another in logwood (§ 78, p. 57), mounting in Canada balsam (§ 96, p. 69).

Appearances under the low power (× 50).—In such a condition there is an increased quantity of blood in the sinuses, and this, stained green, is a very prominent feature. Scattered throughout the green masses in the pulp sinuses are numerous small pink points, which will be recognised as leucocytes. In the Malpighian bodies there is also an increase in the actual size, though this cannot be recognised with the naked eye, and relatively the corpuscle may be smaller. The small round lymphoid cells are numerous, and take on the carmine staining very deeply. Where the Malpighian corpuscles stand out prominently, as in typhoid and scarlet fevers, this increase in the amount of adenoid tissue becomes a very marked feature in the microscopic field. Along the lines of the smaller trabeculæ there is also very frequently a proliferation or exudation of small white cells (stained pink), which arises from the increased blood pressure and other inflammatory conditions.

Under the high power (× 300).—If the congestion is comparatively simple, there may be little more than the distention of the sinuses by red blood corpuscles, with here and there a few colourless blood corpuscles and a number of larger nucleated cells, which appear to be derived from the proliferating endothelial cells lining the pulp sinus. These endothelial cells are all swollen, and appear cloudy; some contain several nuclei, and others contain within their protoplasm a number of red blood corpuscles, or a quantity of golden brown pigment, which is evidently derived from the blood. In the adenoid sheath of the vessel the lymphoid corpuscles are numerous, and in addition, the endothelioid plates, lying on the trabeculæ of the adenoid network, are increased in number, though this condition is

not nearly so marked as in the spleen, in which there is inflammation in addition to the congestion, where, too, the changes in the trabeculæ and sinuses are more distinct. Rapid proliferation of the endothelial cells takes place, and consequent accumulation of leucocytes in the sinuses, exudation of leucocytes along the lines of the trabeculæ, and other evidences of an inflammatory condition ensue. From the inflammation may result abscess formation, which specially affects the Malpighian corpuscles, in which there are rapid accumulation of leucocytes, pus formation, and breaking down of the tissue. The abscesses sometimes appear as small yellow points on the surface of a section, but more frequently they are single and larger. In many cases they are of septic embolic origin, as in acute ulcerative endocarditis, pyæmia, from whatever cause ensuing, and typhoid fever. Such abscesses run an acute course, commencing as dark red hæmorrhagic looking patches, which rapidly suppurate.

Chronic Changes.

210. Where the febrile condition is prolonged, or where there are repeated attacks, as in malarial fevers, the spleen may become permanently enlarged, and it may in such cases be regarded as a typical chronically enlarged spleen. The organ is then firm, and of a dirty greyish red, with pigmented patches seen through the capsule; the capsule is thickened, and running from its deeper layer are numerous thickened trabeculæ. The Malpighian bodies may also be enlarged, but it is often very difficult to distinguish them from the surrounding firm tissue. The pulp is firmer, but very brittle, and not nearly so full of blood as in the normal condition, whilst scattered over the whole of a cut surface are grey, or even black patches, evidently the result of pigmentation. In malarial diseases the pigmentation of the spleen is more marked than in any other chronic form of enlarged spleen; but the enlargement and fibroid change may be noted in a variety of conditions, such as those before mentioned, and in rickets, congenital syphilis, or, more rarely, in the later stages of the acquired form of the last-named disease.

Harden a piece of malarial spleen in Müller's fluid and spirit (§ 54. p. 43), or in methylated spirit (§ 52, p. 42), stain sections in

picro-carmine (§ 73, p. 53) or logwood (§ 74, p. 57), and mount in Farrant's solution (§ 98, p. 71) or Canada balsam (§ 96, p. 69).

Examine under the low power (× 50), and note the thickening of the capsule and of the fibrous trabeculæ, and the increased size of the adventitia of the vessels. The whole pulp tissue is altered, the spaces are not necessarily larger, and frequently they are even smaller than normal, but their walls are thickened. The adenoid sheaths of

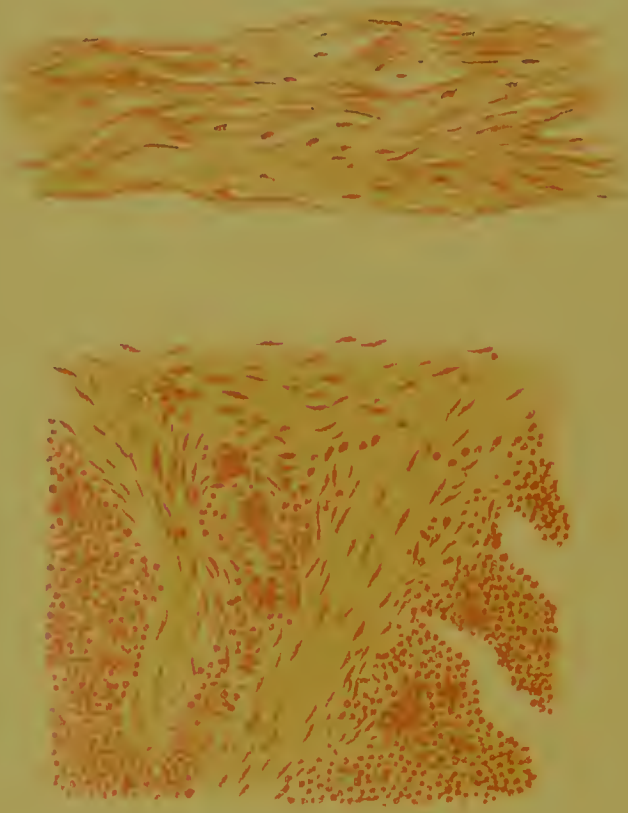


FIG. 73.—Drawing of spleen and capsule in which there was chronic fibroid thickening of the capsule and trabeculæ. Stained with magenta. (× 200.)

f.c. Fibroid thickening of the capsule (flat fibroma).
n. Connective tissue nuclei.
c. Deep layer of the capsule in which are elongated nuclei, some of which are nuclei of non-striped muscular fibres.
t.t. Thickened trabeculæ prolonged downwards from the deep layer of the capsule to which they are similar in structure.
p. Splenic pulp.

the arteries and the Malpighian bodies are pinker and more fibrous in appearance, and the number of small round cells is in many cases

considerably diminished. At the margins of the adenoid sheaths and in the splenic pulp proper are numerous accumulations of pigment, imbedded in the fibrous tissue or in the cells, which can be distinctly seen even under this power.

Under the high power (× 300) observe the thickening of the fibrous capsule and of the trabeculæ, and notice the elongated or rod-shaped nuclei of the hypertrophied bands of the muscular fibre. Mark the more fibrous appearance of the Malpighian bodies, and the large quantities of dark altered blood pigment at the margins of the fibroid masses. Next note the thickened walls of the pulp sinuses, in which the endothelial cells often contain large quantities of blood pigment, as do also the rounded cells lying free in the cavity. There may also be considerable pigmentation of the tissue, of which the walls of the sinuses are composed.

Chronic Venous Congestion.

211. There is another form of the chronic interstitial thickening, which is due more directly to mechanical causes. This condition of spleen is met with wherever there is any obstruction to the outflow of venous blood from the organ. It is consequently found in cases of long-standing heart disease, especially of the mitral valve; in common cirrhosis of the liver, where there is obstruction to the free portal circulation; in fibroid phthisis, emphysema, &c., where there is impeded flow of blood through the lungs, and consequently impaired systemic venous circulation, or where there is direct pressure upon the splenic vein.

The chronic venous congested spleen is enlarged, though often only slightly. It is always heavier, firmer, and more fleshy than normal. The capsule is usually thickened, and, like the liver in this condition, may have villous projections or hard cartilaginoid thickened patches. The cut surface presents a peculiar fleshy appearance, and a bluish red or purple colour; and although, as will be afterwards found, there may be considerable thickening of the trabeculæ, there is no evidence of it to the naked eye. The edge of a cut section is quite sharp and well defined.

Harden a piece of the congested spleen in Müller's fluid (§ 53,

p. 42), stain a section in picro-carmine (§ 75, p. 53), and mount in Farrant's solution (§ 98, p. 71).

Examine a section under the low power (× 50). The changes are essentially the same as those met with in similar conditions in other organs—nutmeg liver (§ 116, p. 94), chronic venous congestion of the kidney (§ 115, p. 178) or lung (§ 198, p. 276).

The large venous sinuses are distended with blood, which is seen as greenish granular material occupying a considerable part of the section. Between the masses of splenic pulp the pink fibrous trabeculæ stand out very prominently, but the adenoid sheaths are not so readily distinguished as in the normal condition. They are more fibroid, and the lymphoid cells are far less numerous. The vessels are seen more distinctly in this condition, as their walls proper are usually somewhat thickened. The cellular tissue of the pulp is very much obscured, but delicate strands of fibrillated tissue may be seen running through the section. These form the walls of the enlarged venous sinuses.

High power (× 300).—The venous sinuses are greatly distended. In them lie numerous coloured blood corpuscles, with here and there a colourless corpuscle, in which may be seen granules of altered blood pigment. The cells lining the venous sinuses are often flattened, and contain altered blood pigment. Between the sinuses there frequently appears to be very little tissue, but careful examination reveals the existence of pink fibrous strands. The Malpighian bodies appear to be fibrous. A few of the lymphoid cells can usually be seen. Perhaps the most marked changes are in the fibrous trabeculæ, which appear to be considerably thickened, and along the lines of the vessels running in them are some leucocytes or small round pink cells. Similar changes may be observed in the capsule. In these two positions there is also marked hypertrophy of the muscular tissue, the elongated nuclei of which can be easily distinguished. Examine the capsule, and note that the cartilaginoid thickenings (Fig. 73) are merely masses of fibrous tissue (the flat fibroma described in the section on tumours). The villous projections are young masses of connective tissue or granulation tissue, with a quantity of lymph on the surface.

Embolic Infarction of the Spleen.

212. In the spleen this infarction occurs in its most typical form. It will therefore be well to take the description of this condition from the appearances here presented.

In its earlier stages the infarction appears as a projection on the surface of the enlarged spleen, running transversely across the convex surface. The projection is not very great, but it is quite sufficient to enable the observer to distinguish the condition. In colour it is deep purple or brick red, according to the stage which the infarction has reached. It is firm, and, on palpation, is readily defined from the surrounding softer splenic tissue. It may pass for a considerable distance into the organ, or it may be situated close to the surface. On cutting into such a mass, it is found to be wedge-shaped, with the rounded base at the capsule, and the apex towards the hilum. The surrounding pulp is highly congested. Of these wedge-shaped masses there are usually more than one—often three, four, or more. Examined at various later stages, the centre is paler, with a yellowish pallor, which spreads towards the periphery, until the whole mass, with the exception of a zone at the outer margin, is entirely involved. The outer congested zone continues for a considerable time, and eventually there is formed in this position a capsule of fibrous tissue, which, as it grows more and more cicatricial, slowly retracts, and draws on the capsule at the margins of the infarct, so that a kind of fossa or ditch is formed around the yellow mass. Following the fatty degeneration, absorption and caseation set in. If the process of absorption continues, the whole of the necrosed tissue is removed, and there is left only a fibrous cicatrix to mark the position of the infarct. In many cases a cheesy mass still remains, surrounded by the retracting fibrous capsule.

Harden a piece of the organ in Müller's fluid (§ 53, p. 42), stain in picro-carmine (§ 73, p. 53), and mount in Farrant's solution § 98, p. 71.

Examine a section taken from an early infarct. In this there is little to be seen beyond an enormous distention of the various vascular channels and sinuses. At a later stage fatty degeneration of these various tissues may be seen towards the centre of the infarct,

especially in a section stained with osmic acid (§ 80, p. 62), whilst at the periphery there is an enormous accumulation of leucocytes or young connective tissue corpuscles in the position of the hyperæmic zone. Later the round cells are organised into connective tissue, which becomes more and more fibrous, and forms bands of distinctly pink stained tissue, which run up to a puckering in the capsule around the caseous mass—at this stage a mass in which pigment granules, and granules and globules of a fatty nature, are the principal constituents; but crystals of cholesterin, hæmatoidin crystals, some fat crystals, or even calcareous salts, may also be found. The salts disappear on the addition of hydrochloric acid. Pigment granules are also to be seen in the fibrous capsule, especially on its inner surface.

Waxy Sago Spleen.

213. Waxy degeneration occurs in the spleen more frequently than in any other organ in the body, with the sole exception of the kidney. It takes one of two forms—the sago spleen, in which the process is confined to the adenoid sheaths of the vessels, the Malpighian corpuscles; or the diffuse form.

In the sago form, the spleen is usually somewhat enlarged, though this is not invariably the case. The organ is hard, firm, and elastic, and in this respect resembles the liver in the waxy condition. On section, the general appearance varies in different cases. In some cases, where there is a large quantity of blood in the organ, it is red, and the Malpighian bodies appear as dark shining masses studding the surface. They are transparent, and gelatinous in appearance, and have been, not inaptly, compared to grains of boiled sago. In other cases the pulp is paler, and then the Malpighian corpuscles appear lighter in colour. In all cases the sago-like masses stand out very prominently as gelatinous looking nodules, which, on the addition of iodine (§ 77, p. 61) give a mahogany brown reaction; and the surrounding healthy tissue gives a yellow reaction. (For other reactions see § 76, p. 59, *et seq.*)

Harden a piece of the organ in methylated spirit (§ 52, p. 42), cut sections (§ 67, p. 48), mount one unstained in Farrant's solution (§ 98, p. 71), stain one in iodine staining fluid (§ 77, p. 61), a second

in methylaniline violet (§ 76, p. 59), a third in iodine and sulphuric acid (§ 78, p. 62), and mount the two latter in Farrant's solution (§ 98, p. 71).

Low power (× 50).—As might be expected from the naked eye appearances, the changes in this condition are confined almost entirely to the Malpighian bodies. Each Malpighian body is stained

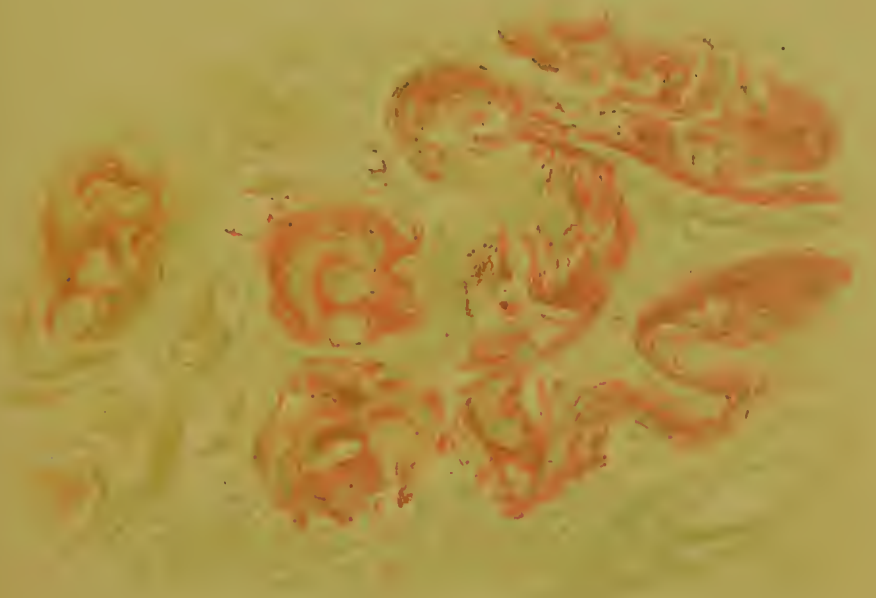


FIG. 74.—Waxy sago spleen. Stained with methylaniline violet. (× 30.)

l.a. Large arteriole, giving off branches around which the waxy adenoid sheath is readily seen.

m.b. Malpighian body or adenoid sheath with (*c.a.*) its healthy arteriole in the centre; the two seen here evidently near the point of bifurcation of the arteriole.

a. Small waxy vessel in the splenic pulp.

p. Splenic pulp.

red violet, with the exception of a small blue ring in the centre, surrounded by a thin zone of blue tissue. Where the condition is very advanced, the red violet mass appears to be almost homogeneous; but at the margins, either near the central blue patch or at the periphery, delicate lines may be seen running from the solid mass into the surrounding blue tissue. The solid looking masses are the Malpighian bodies. The central blue ring is the central arteriole, as yet unaffected, and surrounded by a thin zone of comparatively healthy adenoid tissue. Around the waxy Malpighian body the splenic pulp

(sinuses, cells, &c.) is unaffected, and is stained blue. Running from the margins of the waxy mass are small capillary vessels, the walls of which are undergoing the waxy change, and they consequently appear as the thin red violet lines already mentioned. A more careful examination of the splenic pulp reveals a few small red violet lines, rings, and dots running through it. These are evidently sections of blood-vessels — small arterioles — which have undergone the waxy change. In an iodine stained section, examined by reflected light, the parts before seen as red violet appear brown, whilst the blue parts are canary yellow in hue. In an unstained section the waxy parts are glistening, translucent, and hyaline in appearance, and have a faint yellow tinge.

Under a high power (× 300) examine first the central artery of the Malpighian body. Unless the case be very far advanced, the walls are quite healthy and are stained blue; the intima is thrown into folds by the contracting muscular coat, from which it may be inferred

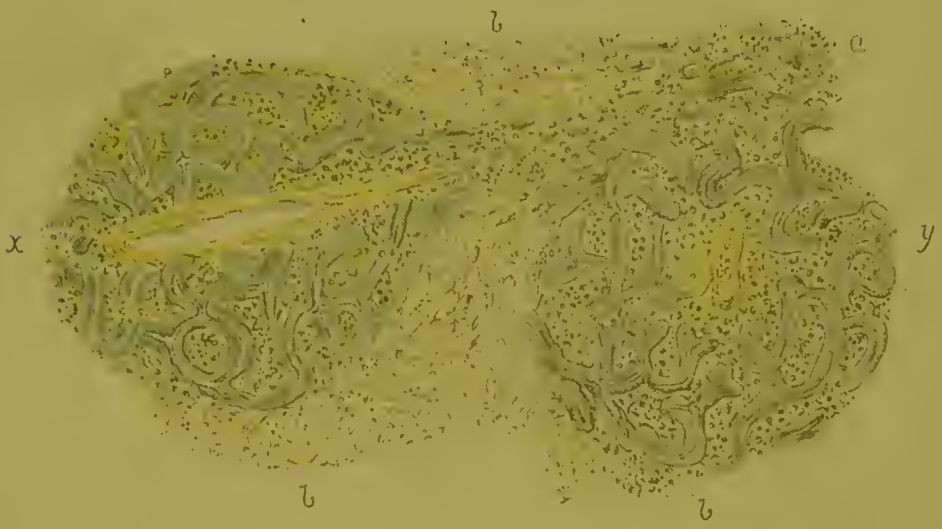


FIG. 75.—Waxy sago spleen, early stage. Stained with iodine and sulphuric acid. (× 70, after Kyber.)

x. and *y.* Enlarged Malpighian bodies, in which the thickened waxy vessels may be seen stained blue.

a. Smaller part of the Malpighian body, in which the central artery is not seen.

b. Splenic pulp unaffected by the waxy disease.

that the muscle is functionally as well as optically healthy. As yet, too, there is no change in the adventitia, and it is only at some little dis-

tance from the vessel that any change is noticeable. The change commences evidently in the walls of the capillary vessels, which run through the Malpighian body, and the vessels are seen as thin, homogeneous, red violet lines, between which the adenoid cells of the sheath, stained blue, stand out prominently. Further outwards, the vessels are more affected, and not the vessels only, but the delicate strands of fibrillated

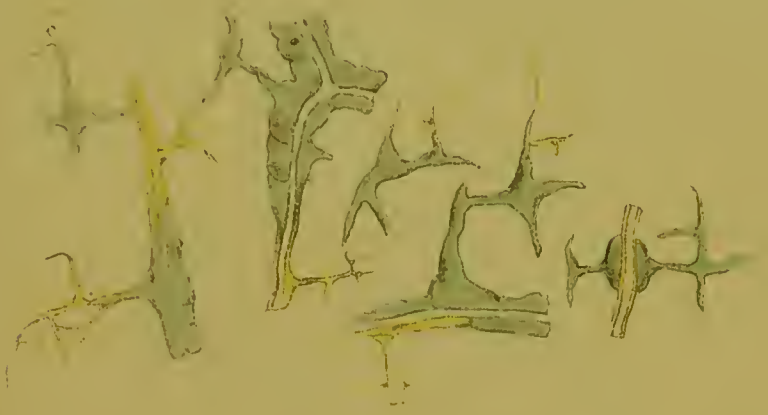


FIG. 76.—Drawing of small capillary vessels and connective tissue fibrils undergoing waxy degeneration, stained with iodine and sulphuric acid. (× 600, after Kyber.)

These vessels were isolated by pencilling from one of the Malpighian bodies of the spleen from which Fig. 75 was drawn.

The degenerated parts are stained blue; the unaffected connective tissue fibrils and capillary walls are stained yellow.

tissue which compose the network of the adenoid tissue. The strands are swollen, homogeneous in appearance, and are stained red violet. Most of the cells between them are comparatively healthy, and are stained blue; but where the condition is very far advanced some of the cells are waxy, or the swollen vessels and fibres have, by pressure, caused atrophy of the cells. Certain it is that the cells are not at all readily discerned. At the periphery of the Malpighian body, the delicate waxy bands are more readily distinguished, and the process may be seen to extend for a short distance in the walls of the vascular sinuses beyond the Malpighian body, where there is a condition very similar to the form of waxy disease, which will next come under consideration.

Running through the blue splenic pulp are numerous small arterioles, the walls of which are in an advanced stage of waxy de-

generation, and the walls of some of the sinuses may be slightly affected. Where this waxy degeneration in the wall of the sinus has once set in, there is usually fatty degeneration of the endothelial cells forming the lining of the sinus. In this position, perhaps, better than in any other, may the waxy change in the vessel be seen.

Examine under a high power, and note—(*a.*) That the waxy change is confined to the middle coat, especially during the early stage of the disease; (*b.*) That the middle coat is picked out in patches by



FIG. 77.—Drawing of a vessel in which the middle coat is slightly affected. Stained with methyaniline violet. (× 600.)

m.f. Circular muscular fibres of the middle coat cut transversely.
w.c.f. Between the muscular fibres the connective tissue fibrils are swollen and waxy, stained red violet. Within the vessel the nuclei of the endothelium are readily recognised.
c.t. Connective tissue corpuscles.
f.c. Fat cells.

the disease; (*c.*) In these patches the tissues are not affected throughout, for on careful examination it will be seen that only between the

muscular fibres is there the waxy change, the longitudinal or transverse sections of the muscular fibres are stained blue, and between them are red violet streaks, which are evidently the swollen connective tissue fibrils. As these are more and more swollen, the muscular fibres become atrophied by pressure, and may ultimately be obliterated. Later, the intima is involved, but never the endothelial lining of the vessels, though it becomes granular and fatty. Here, then, is a condition in which the waxy disease affects specially the walls of the small arterioles soon after they are given off from the large central arteriole, afterwards the connective tissue fibrils around them, and it is possible that, lastly, the adenoid cells may be involved. At the margin of the Malpighian body the walls of the sinuses are affected, but not extensively. In the pulp the small arterioles and a few of the sinuses are seen to be in a waxy condition.

Diffuse Waxy Spleen.

214. This is usually stated to be an advanced form of the foregoing, but it is not by any means invariably the case. Where it is simply an advanced sago spleen, the Malpighian bodies are most markedly affected, but the walls of the sinuses of the pulp tissue become involved in their whole extent. In the true diffuse waxy spleen the change is confined almost entirely to the pulp tissue, and the Malpighian bodies are apparently considerably atrophied.

Naked eye appearances.—The spleen is very greatly enlarged, much more so than in the sago form. Its substance is firm and elastic, and the margins, as in waxy liver, are somewhat rounded. On section, the surface has the peculiar glistening appearance so characteristic of the waxy disease in all organs. The edges of the section are sharp and well defined, and the colour is usually a deep red. The trabeculæ and Malpighian corpuscles are very indistinctly seen, except in an iodine stained specimen, where they may frequently be distinguished as yellow points with a mahogany brown centre. The yellow points are on all sides surrounded by a mahogany brown glistening material, which is at once recognised to be due to an advanced stage of waxy degeneration. It will be noted that the central mahogany brown point corresponds to the arteriole, the yellow area around it to the

Malpighian sheath, and the mahogany brown mass around this again to the waxy degenerated splenic pulp.

Harden a piece of the organ in methylated spirit (§ 52, p. 42), and then treat as for waxy sago spleen (§ 213, p. 312).

Low power (× 50).—Examine the methylaniline violet stained specimen, and note that in many parts of the section the Malpighian bodies are quite unaffected, though in some instances there is a thin ring of red violet material near the central arteriole, in which position it will be observed that the adenoid sheath is most fully developed. Around this the Malpighian body is stained blue, and appears to be somewhat fibroid. The number of cells in some cases is greatly diminished. The pulp tissue is the part affected by the waxy change. The walls of the sinuses are in an advanced stage of waxy degeneration, and are stained red violet; even under this power they are homogeneous and glistening. Within the sinuses the endothelial cells may be seen as small blue granules, whilst the coloured and colourless blood corpuscles may be seen lying in the spaces.

On making a more careful examination under a high power (× 300), the central artery of the Malpighian body is frequently, though not invariably, found to be undergoing waxy degeneration. Sometimes it appears to be perfectly healthy. Around the affected arteriole the capillaries in the Malpighian body may be undergoing the waxy metamorphosis, but the process seldom extends beyond the immediate neighbourhood of the central vessel. The remainder of the Malpighian body is fibroid, and may be considerably atrophied, in which case the lymphoid corpuscles are particularly scanty. At the margins of these Malpighian corpuscles the waxy change commences at once. It appears to take the form of swelling of the fibres of the trabeculæ, which are in immediate contact with endothelial cells lining the pulp sinuses. Around the venous sinuses the bands of yellow elastic fibre (the fibres resembling barrel hoops) are seen on section to be considerably swollen and undergoing the waxy change. The rounded cells situated between the sinuses are atrophied, or fatty and granular, though some appear to be swollen and waxy. This latter appearance is very difficult to determine, and it is just possible that the swollen masses may be sections of some of the swollen

fibrous bands. Examine the endothelial cells, many of which are in immediate contact with the swollen walls. These cells do not take on the waxy reaction with methylaniline violet, but give a blue colour.

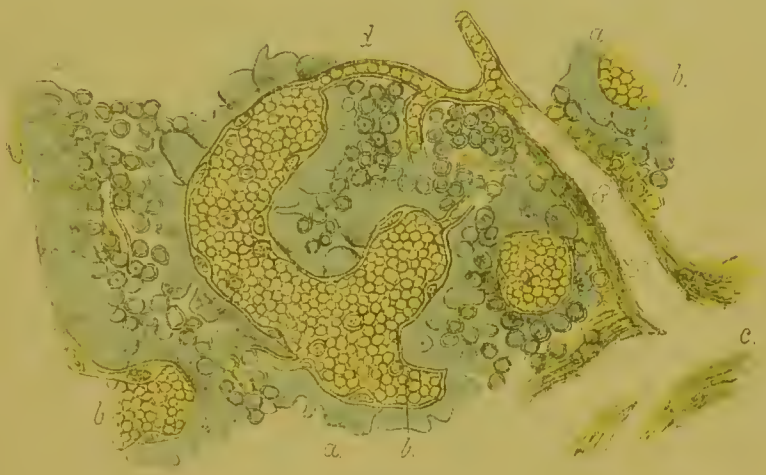


FIG. 78.—Drawing of diffuse waxy spleen, stained with iodine and sulphuric acid. (× 400, after Kyber.)

a. Waxy splenic pulp (between the Malpighian bodies).
b. Venous sinuses lined with unaltered endothelial cells.
c. Small arteriole, unaffected.
d. Capillary opening into the venous sinus.

Nevertheless, they are sometimes extremely granular and fatty in appearance; and this appearance may be more readily brought out by the addition of osmic acid (§ 80, p. 62). In other cases the cells are greatly atrophied, and are detached from the walls of the sinuses. Most of the sinuses are distended with blood corpuscles, both coloured and colourless.

LEUCOCYTHEMIA OF THE SPLEEN.

215. In the spleen the typical appearances of leucocythemia are met with, and a description of the disease, somewhat more full than that given of it as it occurs in the other organs, may here be offered. The spleen is usually enormously enlarged, and may weigh as many pounds as the normal spleen weighs ounces. The enlargement takes place in all directions, so that the organ retains its relative proportions. As in all enlargements of this organ, the notches on the anterior border are strongly marked. The tissue is firm, pale, and tough.

Under the capsule there are sometimes purple patches, the result of hæmorrhages. They stand out very prominently from the surrounding tissues.

On examining a cut surface, it presents a firm homogeneous appearance. The tissues are solid, firm, and pale, but if the Malpighian bodies stand out very prominently from the surrounding mass, the organ appears to be simply hypertrophied.

Examine scrapings from the cut surface under a high power (× 300), and note that it contains numerous leucocytes, a number of coloured corpuscles, and some larger cells, composed of a mass of protoplasm, in which are imbedded nuclei, sometimes a single one, sometimes several. Embolic infarcts, of very various sizes and in different stages of degeneration (§ 212, p. 311), may also be observed as yellow wedge-shaped masses situated near the surface.

Harden one piece of the tissue in Müller's fluid (§ 53, p. 42), and a second in methylated spirit (§ 52, p. 42). Stain a section in logwood (§ 74, p. 56), and mount in Canada balsam (§ 100, p. 72). Stain a second in picro-carmine (§ 73, p. 53), and mount in Farrant's solution (§ 98, p. 71).

Examine under a low power (× 50). Note, first, that although the trabeculæ and Malpighian bodies may be slightly enlarged, they do not form very prominent features in the section. The splenic pulp in the logwood stained section appears to consist of one mass of deeply stained cells, some of which are much larger than the ordinary leucocytes, or even than the endothelial cells in the normal condition. The Malpighian bodies may contain more lymphoid corpuscles, but in certain cases they are more fibroid.

Under a high power (× 300).—Note the above changes in the Malpighian body and in the trabeculæ, both of which may be somewhat hypertrophied. In the Malpighian body the condition varies slightly in different cases. There is an increase in the number of small round lymphoid cells, together with a slight increase in the endothelioid cells, in which case there is, in this position, an increase in the amount of fibrous tissue. These changes are never so well marked as in lymphadenoma, the condition which will be next considered.

Examine the sinuses. The first feature which strikes the observer

is their enormous distention. They are crowded with cells, some of which are indistinguishable from ordinary white blood corpuscles.

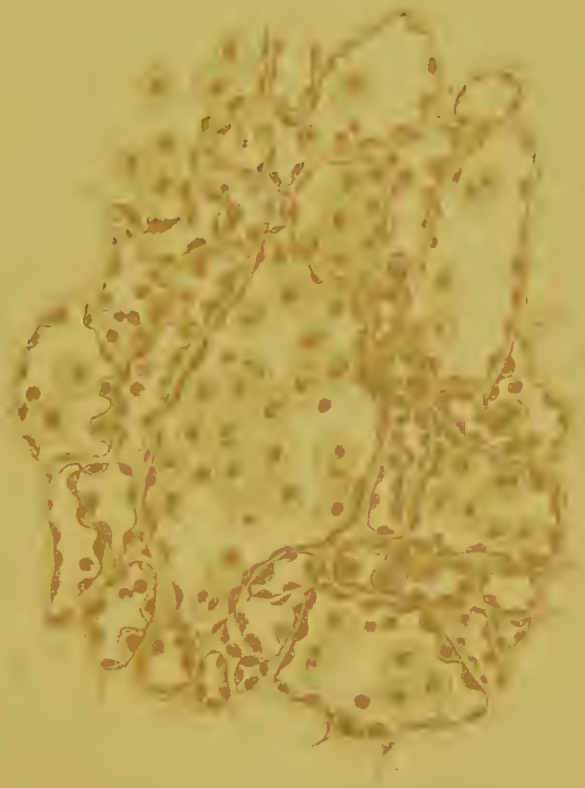


FIG. 79.—Drawing of leucocythemic spleen. Stained with log-wood. (× 300.)

v.s. Large venous sinus lined with a regular layer of endothelial cells, and containing leucocytes (*l.*) and large cells with one or two nuclei each (*c.*).

e.c. Endothelial plates lining the walls of one of the smaller or arterial sinuses.

Along with these are numerous large cells, some of which lie free in the cavity, whilst others are attached by a pedicle to the endothelial cells lining the cavity. In these masses of protoplasm there may be only a single nucleus, but very frequently there are several. The endothelial cells are swollen and multinucleated, and appear on the walls of the sinuses as well-marked projecting masses, to which, as already noted, a number of the larger cells in the cavity are attached. These large cells are in all probability derived from the endothelial cells by a process of proliferation. In them there is usually a quantity of altered blood pigment, and it is confined principally to

these positions, though in some few cases the golden brown pigment granules may be seen lying in the trabeculæ. In other organs there are very characteristic appearances. (See Liver, § 125, p. 120; and Kidney, § 174, p. 221). In the lungs, in the intestine, and on serous surfaces embolic hæmorrhages are usually very numerous in this disease, as are also fatty degenerative changes in the various organs. For a long time lymphadenoma, or Hodgkin's disease, was classed as a form of leucocythemia, and even now the pathological changes are in many text-books stated to be the same. This is an error which must be carefully avoided, as the changes are essentially different in the two conditions. In leucocythemia the changes occur in the splenic pulp, whilst in lymphadenoma the change occurs primarily in the adenoid sheaths of the vessels, and spreads thence until a considerable part of the pulp may be involved. This is merely a continuation of the primary change in the Malpighian corpuscles.

Lymphadenoma of the Spleen.

(*Hodgkin's Disease.*)

216. This disease is found in cases where great enlargement and induration of the various lymphatic glands of the body have been accompanied by no great increase in the number of white corpuscles in the blood. Where the spleen is involved, as is usual in such cases, it is enlarged, though seldom to the same extent as in leucocythemia. In some cases it is stated to weigh from fifty to eighty ounces, or even more.

As in leucocythemia, the increase in size takes place symmetrically, and the notches on the anterior border are well marked. The outer surface is dark in colour, but over the dark surface there are frequently numerous darker spots, purple in colour. The tissue is firm and tough, and in many cases feels quite fleshy, or even fibrous. On section, there is a peculiar and very characteristic appearance. The general surface is deep red in colour, but scattered over it are numerous small angular, translucent, yellow masses, almost like small masses of suet. Some of these are rounded, but others are elongated, branching masses. If it is borne in mind that these are altered

Malpighian bodies, the appearance will be much more easily understood.

Harden a piece of this spleen in methylated spirit (§ 52, p. 42), cut sections (§ 67, p. 48), mount one unstained in Farrant's solution (§ 98, p. 71), and one stained in picro-carmine (§ 73, p. 53) in the same solution.

Under a low power (× 50), the changes are very clearly marked. All the fibrous trabeculæ are increased in size and thickness. They take on the pink stain very readily, and are evidently much more fibrous than normal.

The Malpighian bodies appear to participate in this fibrous change. They are much enlarged, are firm, solid, and fibrous in appearance, and the lymphoid cells are comparatively few in number. Even under this power a few cells may, nevertheless, be seen arranged in rows between the bundles of fibrous tissue cells, which contain several

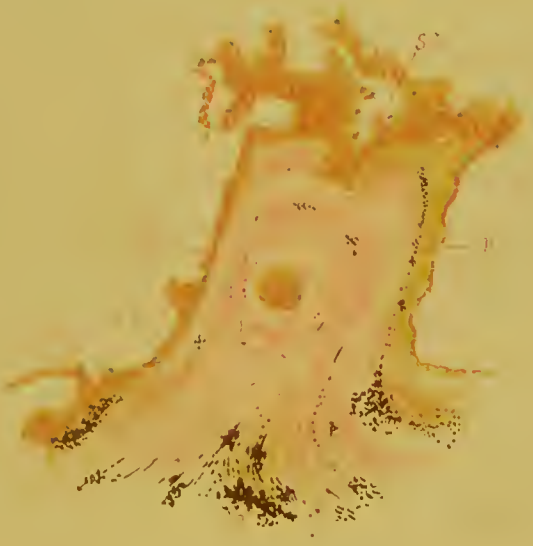


FIG. 80.—Drawing of thickened adenoid sheath in lymphadenoma of spleen. Section stained with picro-carmine. (× 60.)

f.t. Fibrous Malpighian body.
p. Pigment near margin of the Malpighian body.
s.p. Pulp tissue of spleen as yet uneneroached upon.
s.p[1]. Mass of pulp involved by growth of fibrous tissue.

nuclei. These are not the lymphoid cells, but are endothelioid plates, or growing connective tissue corpuscles. At the margin of the fibroid

Malpighian body there is a large deposit of golden brown pigment. This is particularly well marked, and is very characteristic of this condition. It seldom extends far beyond the margin of the mass of fibrous tissue of which the Malpighian corpuscle is now composed. The splenic pulp is considerably altered. It looks much more solid, especially near the margins of the fibriod masses. Away from these the trabeculæ of the pulp are thicker, the endothelial cells are larger, and frequently contain granules of altered blood pigment.



FIG. 81.—Drawing of section of lymphadenomatous spleen. Stained with picro-carmine. (× 250.)

The drawing is taken from the margin of one of the fibrous looking Malpighian bodies.

a. Small arteriole with walls considerably thickened.

b. Well-formed fibrous tissue.

c. Pigmented masses, derived from endothelial and other cells containing coloured blood corpuscles in various stages of alteration.

d. Cells contained within sinuses in process of being cut off by the encroaching fibrous growth.

Under a high power (× 300) all the above changes can be very easily recognised. The Malpighian bodies must be specially observed. They are almost entirely converted into fibrous tissue. The

adenoid cells are few in number, and the few that are present appear atrophied and angular. The spaces between the bands of fibrous tissue are very small indeed, but in them are multinucleated endothelioid cells, which are evidently the cells by which the large mass of fibrillated periplast is formed. The pigment is usually contained in well-defined spaces, and it appears to be derived from altered blood corpuscles. Fig. 81 illustrates the process by which the pigment comes to be situated in the fibrous mass. The fibrous tissue grows in all directions around the central mass, and strands are sent out between the sinuses. These sinuses, with their contained blood corpuscles and endothelial cells, are gradually surrounded. The contained blood corpuscles are disintegrated probably by the endothelial cells, and the blood pigment is set free. The spaces in which the pigment is deposited were originally pulp sinuses. The various transition stages are represented in the drawing. In the pulp the thickening of the trabeculæ and the proliferation of the large endothelioid cells are easily distinguished; but there is no cramming of the pulp sinuses with white blood corpuscles, as there was in the case of leucocythemia.

Tubercle of the Spleen.

217. Tubercle seldom or never occurs in the spleen as a primary growth. It occurs usually in one of two forms; either as minute grey, gelatinous, prominent shot-like bodies in the capsule of the spleen, or near the surface of the organ—a minute yellowish point in the centre of this small mass usually indicates the presence of caseation—or as larger caseous masses. The first form is met with as a local manifestation of a general disease, and hence is of comparatively little importance. The structure under the microscope resembles that of the tubercle in other organs of the body, and the process of caseation is seen to be commencing wherever the yellow points were observed in the naked eye examination.

For examination harden in absolute alcohol (§ 51, p. 42), and a second piece in Müller's fluid (§ 53, p. 42); stain in picro-carmine (§ 73, p. 53), or logwood (§ 74, p. 56).

Along with tuberculosis there is frequently some congestion of the spleen, which, when present, should be carefully observed.

The second form of tubercle is the more typical, especially in children. In this the spleen may be either enlarged or diminished in size. The pulp is usually red and congested, whilst scattered over the red surface are bodies which can scarcely be distinguished from the suet-like masses seen in lymphadenoma; but, as a rule, they are more yellow and caseous looking. They are about the size of a small pea. The organ in this condition is, like the lymphadenomatous spleen, frequently spoken of as a hardbake spleen.

Prepare as above, and note that the appearances are simply those of caseous tubercle.

Other growths mentioned as occurring in this organ are *secondary cancers* and *sarcomas*, *syphilitic gummata*, *hydatid cysts*, one case of *dermoid cyst*, *simple serous* or *mucous cysts*, and one case of *Pentastomum denticulatum* within a calcified cyst.

CHAPTER IX.

THE ALIMENTARY CANAL.

Diphtheria of the Pharynx.

218. In this condition there is exudation of a false membrane on to the mucous membrane of the upper part of the pharynx, palatal arches, tonsils, and especially on the posterior surface of the soft palate or uvula. The last-named is one of the best positions in which to examine the membrane in this disease. The appearances vary according to the date of the disease at which the patient succumbs. If there are simply swollen greyish patches scattered over a dull red background, the epithelium may still remain, though it will be found to be very much altered.

Harden a section in absolute alcohol (§ 51, p. 42), stain in methylated aniline violet (§ 76, p. 59), and mount in glycerine.

In the affected area the following appearances may be noted under a high power (× 300). Usually on the surface, and extending for some distance into the tissues, are masses of micrococci, which take on the methylaniline staining very deeply. The epithelium forms merely a heavy network, of which the margins of the cells apparently form the meshes. Beneath this altered epithelial layer the connective tissue is infiltrated with fibrin and leucocytes, most of which are accumulated around the distended blood-vessels. Around these distended vessels, too, hæmorrhages are frequently seen, but there are as yet few masses of micrococci in the lymphatics and in the deeper tissues generally, and the cell infiltration is confined to the tissues immediately beneath the epithelium or the point of infection.

At a later stage, where the false membrane has formed, and perhaps has sloughed, leaving a grey, sodden, sloughy, and infiltrated looking surface, a piece of the tissue must be treated with alcohol

and methylaniline violet, and examined microscopically. The following appearances may be distinguished :—The grey sloughy part is

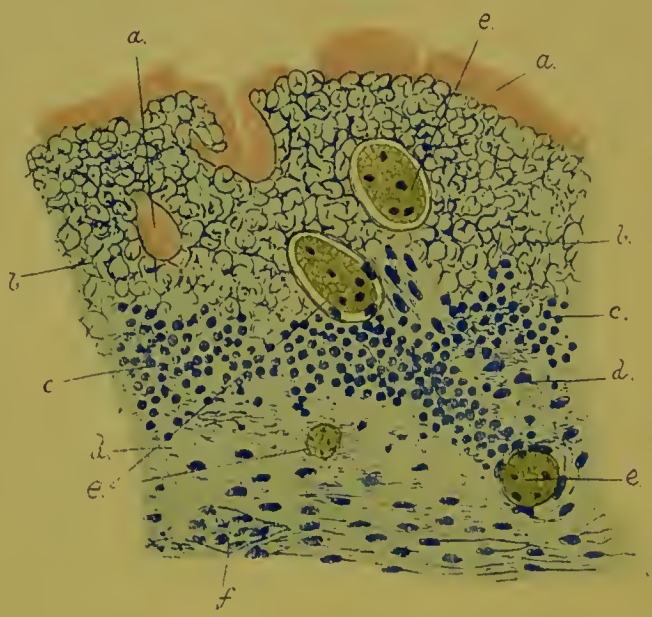


FIG. 82.—Section of uvula, from which the epithelium has been detached, from a case of diphtheria, stained with methylaniline violet. (× 100, after Ziegler.)

a. Micrococci.
b. Amorphous submucous tissue.
c. Leucocytes infiltrating tissue.
d. Fibrinous exudation.
e. Blood-vessels.
f. Lymphatic vessel, in which are accumulated small round cells and fibrin.

usually teeming with masses of deeply stained micrococci, but there is now no trace of epithelial structure left. The connective tissue is transformed into a mass of fattily degenerated or homogeneous material, which is very characteristic of the diphtheritic condition, infiltrating the connective tissue. A fibrinous exudation, in which the masses of micrococci are situated, often forms a false membrane on the surface. The blood-vessels are distended, and are surrounded by a number of round cells or leucocytes. This accumulation of cells takes place especially at the point of junction between the submucous and the deeper tissues. There is a further quantity of fibrinous lymph, in which are few leucocytes. The lymphatics for some distance round are choked with this lymph, or more frequently with masses of micrococci. Micrococci may be found in any part of the slough. The distinctive characteristics between this condition and the

so-called croup are, that in diphtheria the micrococci and the slough are always present, but the fibrinous exudation, though usually present, is not essential; whilst in croup the exudation is essential, and the micrococci, if present, are found only on the surface, do not invade the membrane or the surrounding lymphatics, and so do not get into the system to give rise to constitutional symptoms.

Harden in absolute alcohol (§ 51, p. 42) a lymphatic gland of the neck—say from a case of diphtheria—stain section in methylaniline violet, and mount in Farrant's solution or Canada balsam.

Examine under the low power (× 50), and observe the masses of micrococci in the cortical part of the gland. Notice, too, the green masses in the same position.

Examine further under the high power (× 300). The masses of micrococci can be readily distinguished, and the green masses are seen to be hæmorrhagic collections in the follicles of the cortex of the gland.

The Stomach.

The stomach is one of the least satisfactory organs with which the pathologist has to deal. *Post mortem* changes take place so rapidly in the organ, that any changes of recent date are at once masked, and even those of longer standing are considerably altered. It is, therefore, impossible to give an exact and non-arbitrary account of either the naked eye or microscopic appearances in many diseased conditions. A description of the most typical simple ulcer of the stomach —an ulcer which is met with most frequently in chronic dyspeptics— must suffice.

"Common," "Chronic," "Circular," "Perforating," or "Simple" Ulcer of the Stomach.

219. This form of ulcer is usually single, though from two to four sometimes occur. It is situated in most cases on the posterior wall, or on the lesser curvature of the stomach, and measures from one-half to two-thirds of an inch in diameter. Its appearance is very characteristic. The edges are seldom much injected or raised from the surrounding tissue, the margins are quite vertical, and the floor is smooth. The form

of the ulcer is rounded or oval, and the formation gives one the idea that it might have been punched out with a wad-punch. The depth varies greatly in different cases. In some instances the mucous membrane only is involved. The punched-out appearance is in such cases very well marked. If the ulcer extends deeper, so as to eat through the muscular coat, there is a peculiar terraced appearance, as though a smaller punch had been used for the deeper layer. Where perforation takes place, it may be by only an exceedingly small hole. Where acute ulceration has ceased, but the ulcer does not heal, there may be slight thickening of the surrounding tissues, and of such a thickened ulcer are the microscopic appearances about to be described. Harden in Müller's fluid (§ 53, p. 42), or in absolute alcohol (§ 51, p. 42), cut sections through the ulcer and a quantity of the surrounding tissue, stain in logwood (§ 74, p. 56) or picro-carmine (§ 73, p. 53), and mount in Canada balsam or Farrant's solution.

Under the low power (× 50).—Around the ulcer, in its immediate neighbourhood, there is a considerable increase in the number of small deeply stained cells, whilst in the mucosa and submucosa, a little further away, there is also an increase in the number of the small round cells; but the glands supported by this tissue are little altered, except that they stand out more prominently than in the normal condition. Further changes are described by Cornil and Ranvier as thickening of the walls of the vessels near the ulcer and diminution of their calibre; and where the muscular coat is invaded, fatty degeneration and fraying out of the muscular fibres are also described. These appearances are naturally more easily recognised under the high power (× 300).

When these ulcers perforate, they may open into the peritoneal cavity, into the pancreas, liver, or spleen, or into some of the surrounding blood-vessels, as the coronary arteries or the splenic vessels. (A very good example of this is to be found in the pathological collection in the Anatomical Museum of the University of Edinburgh). Even after perforation the ulcers may heal. The new tissue gives rise to a cicatricial mass, and the ulcer, contracting, heals, and leaves a puckered or radiate scar. Where the ulceration is not extensive, healing may take place so perfectly, that no scar can be distinguished without a very careful examination. This applies especially to those

cases where, whilst the course of the case has been acute, the destructive process has not been extensive. It is necessary to mention the supposed cause of this disease, and to connect the described condition of the vessels with the ulceration. It is generally agreed that the solution of continuity is due to the cutting off of the blood supply from a certain area, and that this area, deprived of its nutrition, is acted upon by the gastric fluids and softened. That the process is acute is also agreed, but there is some difference of opinion as to the cause of obstruction to the flow of blood. Spasm of the vessels, atheroma, embolism, &c.—each has its advocates; but it appears probable that any of these may cut off the blood supply, and so permit the digestive process to take place upon the patch of tissue originally supplied by the obstructed vessel.

Several of the cicatrices may occur, especially in the middle of the stomach, when by their contraction they give rise to what is known as the hour-glass stomach. Similar ulcers are found in the duodenum.

Tumours met with in the Stomach.

220. *Sarcoma* is very rare. *Fatty tumours*, *papillomas*, *myomas*, *fibromas*, *lympho-sarcomas*, and *cancers* are of more frequent occurrence, especially the last named.

Cancers are very frequently primary, and usually occur at the pyloric end of the stomach.

Scirrhous, encephaloid, colloid, and adenoid cancers are all met with in this position. They will be described generally under the heading of tumours, but in cancer of the stomach the tendency to softening and hæmorrhage must be especially borne in mind. Infiltration of the submucous tissue with the cancerous material is frequently very clearly marked. In most cases of cancer of the pyloric orifice there is naturally catarrh of the stomach, with dilatation and hypertrophy of its muscular walls.

Typhoid Lesion of the Intestine, leading to the formation of the Typhoid Ulcer.

221. In this condition there is first marked swelling of the glandular elements in the submucous tissue of the intestine, the solitary glands, or

the groups of them known as Peyer's patches. The disease is therefore most marked in those positions where the glands are most numerous, and consequently it is most advanced at the lower end of the ileum. The disease may spread upwards, and, though rarely, downwards. In the earlier stages of the disease, during the first week, there is a progressive swelling of the solitary glands, which at first are soft and pulpy in appearance and to the touch, but later they become firmer. All the Peyer's patches at the lower part of the intestine become involved throughout their whole extent, as also do the solitary glands. These patches are sharply raised. On their surface the mucous membrane is swollen and smooth, and is frequently somewhat paler than the surrounding tissue, though in the earlier stages the patches are very vascular, and there may be even small hæmorrhages from the deeply congested surface.

If a piece of the intestine with one of these patches be stretched out on a piece of flat wood, held in position with tacks, and then hardened in absolute alcohol (§ 51, p. 42), sections may be made, and the following appearances observed.

The gland is swollen, and projects into the lumen of the intestine, pushing before it the mucous membrane. The swelling is composed of round cells or leucocytes, which also to some extent infiltrate the surrounding mucous and muscular tissue. If a small portion of the swollen gland be teased out, a number of much larger multinucleated cells, derived from the endothelial cells of the gland tissue, are brought into view. It is stated that rod-shaped bacilli are present during this stage of the process, both in the adenoid tissue of the mucous membrane and in the mesenteric glands. To see these, fresh scrapings must be stained with methylaniline violet, and mounted in Farrant's solution or Canada balsam.

When these masses have become very tense and pale, the stage of sloughing sets in. The slough involves the mucous, and usually also the submucous tissue. It is invariably bile-stained, and very frequently blood-stained also, from rupture of some of the small blood-vessels in the muscular coat. It comes away in fragments; and if violence of any kind is used, the slough dragged away from the softened tissues beneath may cause their laceration, and so bring about perforation of the intestine. It will be noticed that, although all of

the glands and patches are swollen, comparatively few are ulcerated; and even those that ulcerate may not slough throughout their whole



FIG. 83.—Diagram to represent the various stages of the typhoid lesion in Peyer's patches. (After Thierfelder).

a. Section through the patch in the early or swollen stage.
b. Stage at which a line of demarcation is forming between the slough and the subjacent tissue.
c. Ulcer from which the slough has separated. The walls of the ulcer are vascular and infiltrated.

extent. In the Peyer's patch, for instance, the ulcer may involve the central width of the patch, but may extend for some distance on each side, as one would be led to expect from the infiltration of the neighbouring tissues. On the other hand, the ulcer very frequently has the shape of the Peyer's patch, or of the solitary gland, as the case may be. Where the whole of the patch is involved the ulcer is oval in shape, and the long axis of the ulcer corresponds to the long axis of the bowel. The floor of the ulcer, which is usually composed of the circular muscular coat of the intestine, is smooth, injected, and glossy, but there is comparatively little thickening. The margins of the ulcer are somewhat ragged, are much undermined, and can be readily floated out in water. They are composed of the mucous membrane and submucous tissue, though where the ulceration has extended, as in some cases it does through the circular muscular coat, the longitudinal fibres may form the floor of the ulcer, and the free ends of the circular fibres may then form part of the overhanging margins. There is no thickening of the peritoneum in this condition.

This ulcer may heal without leaving a marked cicatrix, the edges simply falling down and uniting with the floor, in which case there is

no new formation of glandular tissue. On the other hand, the ulcer may go on to perforation by extension of the ulcerative process, in which case it is frequently accompanied by hæmorrhage.

Harden a piece of the intestine, stretched out on a piece of wood, in absolute alcohol (§ 51, p. 42), stain a section in picro-carmine, (§ 73, p. 53), and mount in Farrant's solution.

Under a low power (× 50), note the shape of the ulcer, the overhanging margins, with the follicles and papillæ of the mucosa on the upper surface.

In all the tissues bounding this ulcer, the overhanging walls, and the smooth muscular floor, there is evidently a considerable amount of small cell infiltration, but this does not give rise to any very great amount of thickening. These appearances must be confirmed under the high power (× 300). The mesenteric glands and the adenoid corpuscles of the spleen must also be examined for similar congestion, and for infiltration with round cells and multinucleated endothelioid cells.

Tubercular Ulcer of the Intestine.

222. Tubercular ulcers are found especially in connection with the solitary glands and Peyer's patches, but they are not confined to these positions. They most frequently occur at the lower end of the ileum, but may extend above this point, and down below the ileo-cœcal valve. In its most common form the tubercular ulcer is met with in very nearly half the cases which succumb to chronic phthisis. The first evidence of the process is the appearance of small greyish or yellowish points in the substance of the glands, or in the submucous tissue. These rapidly undergo softening, the mucous membrane above them sloughs away, the caseous material is evacuated, and a small deep ulcer remains, with thickened overhanging edges. Several of these ulcers may be found situated near to one another, separated by strips of thickened mucous membrane. They extend laterally until they merge into one another, and a large ulcer is formed, which again spreads by a similar process. In consequence of this method of formation, the larger ulcer, which usually runs transversely to the long axis of the bowel, "presents a sinuous or scalloped

outline."—(Bristowe.) The ulcer may spread so as to encircle the intestine. The margins of such an ulcer are thickened and infiltrated. In addition to the general infiltration, there are numerous caseous tubercular nodules, which give the thickened edge a nodulated appearance. There is usually no great undermining of the edges, as in typhoid ulcer. The edges may even be terraced, especially in the smaller forms. The floor and edges are pale in the majority of cases, but there may be slight injection extending from the floor, which is usually somewhat vascular, roughened, and nodulated. The nodules are most frequently tinged with yellow, from caseation or bile staining, or both. Though the ulcer usually runs transversely to the long axis of the bowel, it may run in the direction of the long axis.

Examine the serous surface, and note the following appearances. Immediately under the ulcer, or situated in its floor, are numerous firm grey or yellowish rounded bodies, which are evidently situated along the lines of the subserous lymphatics. Radiating from the floor are similar lines of tubercle nodules, forming a many rayed star, the centre of which is situated immediately beneath the ulcer. Between the floor of the ulcer and the serous surface there is considerable thickening, and in the thickened portion the nodules may be felt as hard shot-like bodies. The ulceration usually extends through the mucosa and submucosa, and the muscular tissue then forms the floor. Eventually the muscular tissue also may be involved.

Perforation very seldom occurs as a result of tubercular ulcer of the intestine, and in some cases there may even be cicatrisation of the ulcer. In such a case the contraction is very great, as one would expect from the great loss of substance which takes place. A stellate puckered scar is the result. The puckering is especially well marked on the serous surface. Where the loss of substance has been very extensive indeed, the cicatrisation may cause considerable narrowing of the bowel.

Harden a piece of this ulcer, stretched out on a piece of wood, in absolute alcohol (§ 51, p. 42), stain in picro-carmine (§ 73, p. 53), or as for tubercle (§ 200, p. 282).

Examine under a low power (× 50). At the point where the

ulcer is situated there is particularly noticeable increase in the thickness of the submucosa. The edges of the ulcer are covered with mucous membrane up to its margin; beneath the layer in which the crypts, &c. may be seen there is a very great amount of round

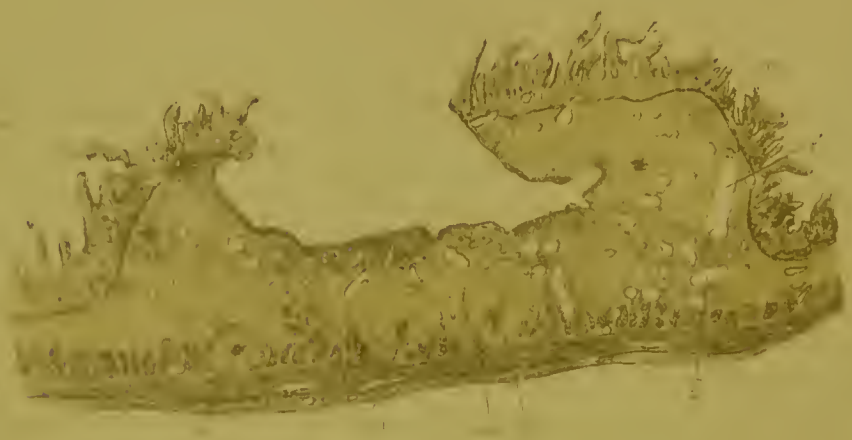


FIG. 84.—Section of tubercular ulcer of intestine—ileum. (× 35, after Thierfelder.)

m.c.	Mucosa, which at points *u.u.* has given way.
v.	Villi, infiltrated and enlarged.
m.m.c.	Slightly altered muscularis mucosæ.
s.m.c.	Submucosa, in which (*u*) the tubercle follicles are present. In this layer too (*g*) the blood-vessels are considerably dilated.
r.m.	Circular muscular fibre at $r.m^1$ swollen and enlarged.
u^1.	Tubercle follicles situated in this layer.
l.m.	Longitudinal muscular fibres.
s.	Thickened and vascular serous coat.

celled infiltration, scattered through which are tubercle nodules composed of one, two, or more tubercle follicles. In the centre of some of these there are evidences of the commencement of caseation. Others are well formed, and present the giant cell system, the reticular framework, endothelioid cells, small cells, and the rest. The floor of the ulcer, which is rough and nodular, is composed of similar structures. The tubercle nodules in some cases extend into the muscular coat, and also extend laterally for some distance. These structures must be further examined under the high power (× 300), and the typical tubercle structure observed (see Liver, § 123, p. 115). The mesenteric glands are in this condition usually affected, and the tubercle follicles grow in the cortical part of those structures. They first enlarge and then caseate.

Typhoid Ulcer.	Tubercular Ulcer.
1. Direction longitudinal (frequently).	1. Direction transverse (frequently).
2. Edges ragged, and can be floated out on water; they are thin, vascular, and undermined, and are composed of mucosa and submucosa.	2. Edges not undermined; margins thick, prominent, nodulated, terraced, or sloping—pale or red.
3. Floor smooth and vascular.	3. Floor nodular, thickened, irregular.
4. Peritoneal surface unaltered, except that it may be inflamed. No thickening and no tubercle.	4. Peritoneal surface—small yellow or grey points in the floor of the ulcer running along the lines of the lymphatics. Peritoneum thickened.
5. Mesentery unaltered; glands enlarged, red, and softened.	5. Mesentery thickened at its attachment to the bowel; glands hard and firm, or caseous.
6. Perforation more common, both by separation of slough and by direct extension of the ulcerative process. Small opening by which fæces escape. Peritonitis. Hæmorrhage may occur during either of these processes.	6. Perforation rare.
7. Microscopically: A specific inflammation affecting the adenoid tissue; blood-vessels distended. Dense masses of small round cells, with some larger multinucleated cells, the latter of which are derived directly from endothelium. Then line of demarcation formed, and abscess succeeds.	7. Microscopically: Vascularity of mucosa and submucosa; increase of connective tissue corpuscles and tubercle masses, typical or caseating. It commences in the mucous membrane, and is due to direct contagion or infection.
8. Extension takes place laterally, or in depth.	8. Extension takes place principally laterally.

Waxy Intestine.

223. Waxy degeneration of the intestine very frequently occurs in general waxy disease; in fact, the watery diarrhœa in such cases is frequently the actual cause of the death of the patient. The disease should first be looked for at the upper part of the ileum and the lower part of the jejunum, though the mucous membrane of the whole alimentary tract may be more or less affected by the disease. The naked eye appearances are characteristic. The mucous membrane is pale, and has a peculiar smooth and glossy appearance, and to the touch it is almost like a piece of fine silk velvet. If a watery solution

of iodine be poured over the surface, a number of dark mahogany brown points make their appearance, corresponding to the vascular loops of the villi. Between these points the normal tissues are stained yellow. Where the large intestine is affected the dark staining is much more diffuse, owing to the absence of villi and the presence of a dense vascular plexus in the mucous membrane. Harden a piece of the waxy intestine, stretched out on a piece of board, in methylated spirit (§ 52, p. 42), stain a section in methylaniline violet (§ 76, p. 59), and mount in glycerine (§ 97, p. 70), or in Farrant's solution. Mount one unstained in Farrant's solution.

Examine under a low power (× 50). The principal position in which the waxy change occurs is in the capillary plexuses of the villi. The vessels of which these are composed have their walls swollen, hyaline, and stained red violet with the methylaniline violet. In consequence of the swelling of the wall, the lumen is considerably narrowed. There are still a few blood corpuscles to be seen in a few of the vessels. The epithelium on the surface of the villi is frequently detached, and is granular, but is seldom affected by the waxy change. Some of the larger and deeper vessels are similarly affected, especially their middle coat. In some cases there is waxy degeneration of the delicate connective tissue fibrils between the bands of non-striped muscular fibre. In advanced cases atrophy of the muscular fibres may be recognised even under the low power.

Examine under the high power (× 300). The evidences of waxy affection of the loops of vessels in the villi may be readily seen. It affects the middle coat, the endothelium remaining fatty. The larger and smaller vessels are similarly affected. The epithelium on the surface of the villi is fatty, granular, and detached, but is rarely if ever waxy. Under the high power the waxy material may be observed between the bands of atrophied non-striped muscular fibre, but the muscular fibres themselves are seldom affected.

Dysentery (Tropical Form).

224. This disease primarily affects the large intestine, especially in its lower part; but it occurs in some cases even higher up in the lower part of the ileum.

The first indication of the diseased process is swelling, accompanied by redness of the mucous membrane, on which a viscid or tenacious mucous material accumulates. The swollen mucous membrane is thrown into folds, and there is vascularity, especially well marked, along the ridges of these folds. At this stage the solitary glands are firm and swollen, and here and there are small hæmorrhages. After a time sloughs are formed, which occupy the ridges of the mucous membrane. Small ulcers are also found in the position of the solitary glands. The sloughs are blood-stained, bile-stained, or ashen grey, and on separating the submucosa is left bare, and very intractable ulcers are formed, which, if the patient lives, give rise to the chronic form of the disease. These ulcers in the acute condition are surrounded by a zone of active congestion, and frequently also by small hæmorrhages. The contents of the intestine in this condition, consisting of mucus, altered blood, and scraps of sloughy tissue, emit a very foul odour. If the shreds of sloughy tissue which have separated from the intestine are carefully examined, they will be found to be teeming with micrococci. In still more acute forms the mucous membrane is deep red or livid looking, and may come away as a complete cast of the bowel, usually accompanied by greater hæmorrhages.

Harden a piece of the acute dysenteric intestine in absolute alcohol (§ 51, p. 42), cut sections, stain in picro-carmine (§ 73, p. 53), and mount in Farrant's solution (§ 98, p. 71); stain a second section in methylaniline violet (§ 76, p. 59), or some other germ-tinting reagent, and mount in Canada balsam (§ 96, p. 69).

The subjoined description is drawn from various sources, as the author has had no opportunity of making special examination of intense dysenteric inflammation of the intestine.

Microscopic examination.—There is first a very great amount of small round cell infiltration in the tissue around the follicles of Lieberkühn. There is similar infiltration of the solitary glands. Near the margins of the ulcers the infiltration is well marked, especially around the distended blood-vessels. Some of the solitary glands are seen to be breaking down, and forming smaller ulcers. The glands of Lieberkühn are elongated, and constricted irregularly, with bulgings at certain points, and the epithelium is frequently in

process of being shed from them. Among the cells around the vessels are the elements of a coagulum, coagulated fibrin, &c. Around an ulcer, both in the floor and in the margins, are numerous round cells, infiltrating the whole of the tissues, whilst large swollen endothelial cells are described as being present in the lymph vessels in the neighbourhood of the ulcer. In the methylaniline stained specimen masses of micrococci are met with, still attached to the surface of the mucous membrane, especially where sloughing is commencing.

Tumours of the Intestine.

225. *Fibroma*, *myoma*, and *lipoma* are all met with in the mucous membrane as polypoid tumours.

Adenoma, both simple and malignant. The latter form, being known as columnar epithelioma, is found especially in the colon.

Squamous epithelioma and scirrhous, encephaloid or colloid, *cancer* occur usually near the rectum.

For *parasites* of the intestine see section on Parasites.

Peritoneum.

226. The peritoneum may conveniently be taken up along with the intestine. It is very easily prepared for histological examination, and will prove a most interesting structure for study. To examine it fresh, cut out a thin piece from the mesentery or the omentum with a pair of fine sharp-pointed scissors, spread out on a slide, stain with picro-carmine (§ 73, p. 53), cover with a drop of glycerine, and put on a cover glass; cement (§ 104, p. 74). If the specimen cannot be mounted at once, transfer to a weak (fifty per cent.) Müller's fluid (§ 53, p. 42), gradually increase the proportion of Müller's fluid for a few days, and then keep in preserving fluid (§ 71, p. 52); mount and treat as above, or stain in logwood (§ 74, p. 56) and mount in Canada balsam (§ 96, p. 69), or in methylaniline violet (§ 76, p. 59), and Farrant's solution (§ 98, p. 71).

Inflammation of the Peritoneum.

227. To the naked eye the appearances are very much like those presented in inflammation of any serous surface.—(See Pleurisy, § 184.

p. 239). In a specimen taken during the early stage of inflammation, stained with logwood and mounted in Canada balsam, the following appearances may be observed under the low power (× 50):—(1) a considerable increase in the number and size of the endothelial cells, some of which are still adhering to the fibrous trabeculæ, whilst others are lying loose in the spaces; (2) an accumulation of leucocytes, which is evidently the result of migration or diapedesis from the venules. Note the position of these masses—the points at which the capillary or smallest veins, after the capillaries, open into the larger venules—*i.e.*, most of the leucocytes are collected in the right angle at the junction of the venules.

Examine under a high power (× 300), and observe the larger endothelial cells bulging from the trabeculæ, then the leucocytes in

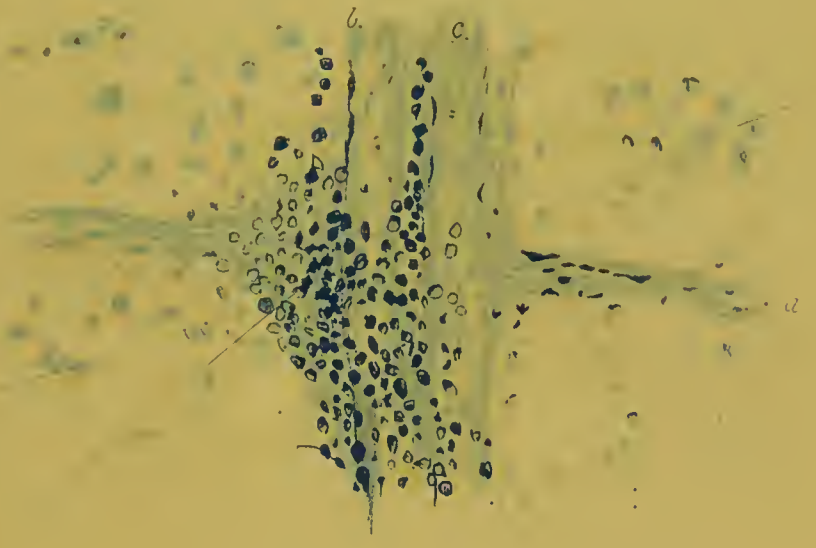


FIG. 85.—Early inflammation of peritoneum. Stained with logwood. (× 300.)

a. Capillaries, arterial and venous.
b. Larger venule.
c. Larger arteriole.
d. Accumulation of leucocytes at the angle formed at the junction of *a.* and *b.*
e. Fibrous trabeculæ of peritoneum.
f. Endothelial cells, proliferated and detached from trabeculæ.

the positions previously mentioned. The larger endothelial cells are frequently multinucleated, and some appear to be undergoing fatty degeneration.

In the later stages, where there is great exudation of lymph and organisation in lymph, the microscopic appearances are very similar to those met with in pleurisy (§ 184, p. 239, *et seq.*)

Tuberculosis of the Peritoneum.

228. A non-caseating tubercular process is very frequently met with in the peritoneum in general tuberculosis of children. This is perhaps one of the best possible positions in which to examine young tubercle.

Hold a piece of the peritoneum up to the light, or lay it out on a dark background, and in it will be seen a number of minute white or

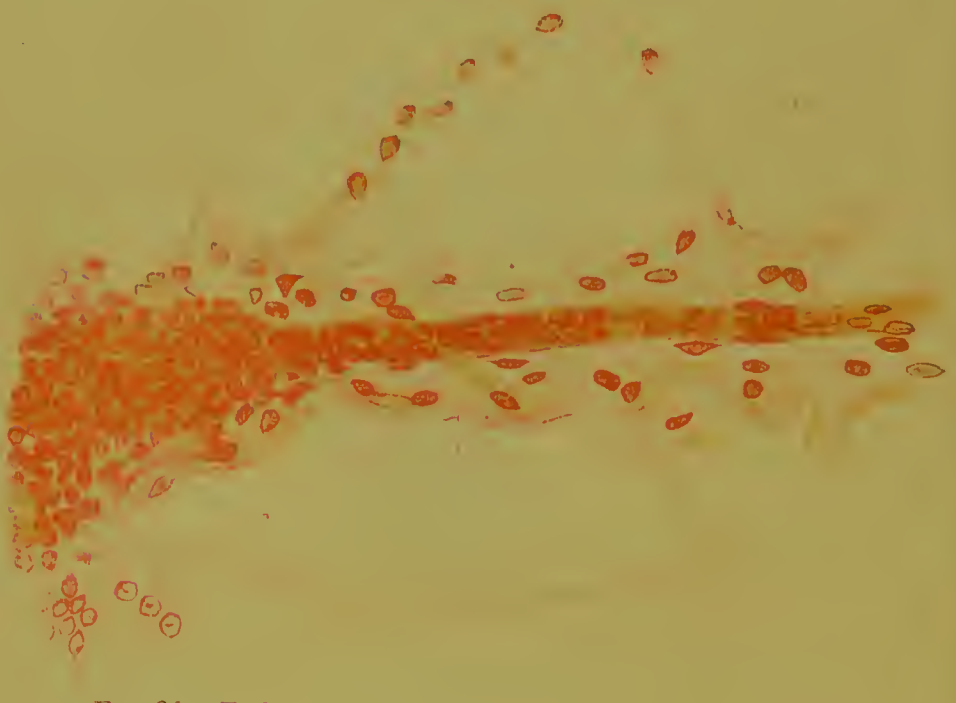


Fig. 86.—Early acute tubercle of peritoneum, from child. Stained with picro-carmine. (× 300.)

a. Young tubercle growth. Endothelial cells growing within the peri-arterial sheath, and also on the peritoneal surface.
b. Artery, along the course of which the proliferating endothelial cells may be seen.
c. Fibrous trabeculæ.
d. Proliferating endothelial cells lying on these trabeculæ.

cream-coloured points, very like those met with in tubercle of the pia mater.

Stain a section in picro-carmine, and mount in Farrant's solution.

Examine under a low power (× 50). Along the course of the small blood-vessels, at irregular intervals, are masses of cells which appear to be enclosed by a boundary line. The cells vary in size; some are small round cells, whilst others are endothelioid, and contain several nuclei. Along with the masses there are lines of cells which apparently still follow the course of the vessel, whilst at other points there appears to be proliferation of the endothelial cells on the trabeculæ.

Under the high power (× 300), it appears that the endothelioid cells in the perivascular lymphatic-spaces are at certain points undergoing proliferation, and that this cell growth is really the early stage of tubercle formation, already described (§ 170, p. 216). It will be seen that there are no giant cells, properly so called, and that the greater number of the changes are taking place at intervals along the line of the artery, but not of the vein.

Chronic tuberculosis, with matting together of the intestines, puckering and thickening of the omentum, occurs very frequently in connection with tubercle of the intestine. The principal features then are, that it is of extremely slow growth, that the giant cells are most perfectly formed, and that it may be accompanied by chronic peritonitis.

The waxy change in vessels may also be readily studied in the peritoneum, as may other vascular changes, as in septicæmia, anthrax, and the rest. *Cancer*, especially the colloid form, and *sarcoma* both occur as secondary growths in this position.

CHAPTER X.

BONE AND JOINTS.

Rickets.

229. In this, perhaps the most common of bone diseases, the changes occur almost entirely during the period of development of the bones. The disease is most frequently met with in badly nourished children, from one year old and upwards. The most marked changes are in the long bones, especially at their points of junction with cartilage. The flat bones of the head, and even the spongy bones of the spinal column, may also be considerably altered. It will be necessary to confine the description to the disease as it manifests itself in the long bones. If the characteristics of the changes are understood in the one position, they will be very readily understood in others.

In a typical rickety bone, such as the radius at its lower extremity, the first point to be noticed is that there is much enlargement of the epiphyseal part of the bone; enlargement is also present at the lower end of the bone above the epiphyseal cartilage, which cartilage frequently forms a layer of considerable thickness. If the muscles be stripped from the bone, the periosteum being left attached, if possible, it will be found that the periosteal layer is thickened and very vascular, and that the bone, in place of being dense, is almost like the spongy bone of the extremity. The transverse diameter of the shaft is usually considerably increased; but, in spite of this, the bone of which this is composed gives way more easily than does the normal bone.

If a vertical section be made through the shaft with its epiphysis, and the enlarged end examined, the first thing to be noticed is the great increase of the translucent or bluish cartilage; this, in place of forming a thin regular layer, either on the articular surface

or between the epiphysis and the shaft, is seen as a broad irregular belt, dipping into the calcifying tissue, and small islets of calcifying tissue are scattered irregularly throughout. With the advent of the calcifying centres there is usually increased vascularity, so that with the small yellow centres in the blue mass pink points are seen. On section the shaft is red and vascular, the bony lamellæ are thin and friable, and the proportion of marrow is relatively large. In consequence of these changes the bones are very soft and pliable, and are readily bent. Infractions, or greenstick fractures, frequently take place, especially in the upper limbs, and the epiphyses are often displaced. They become clubbed at the ends, and are usually much shortened and curved, in addition to being thickened. The curve is merely an exaggeration of the normal curve of the bone.

Treat pieces of the cartilage and bone from the lower end with picric acid (§ 62, p. 46), and a small piece of the shaft, with the periosteum attached, with chromic and nitric acid fluid (§ 63, p. 46), make sections (§ 67, p. 48), stain in picro-carmine (§ 73, p. 53), and mount in Farrant's solution (§ 98, p. 71).

Under a low power (× 50) examine the cartilage with the irregular calcareous and bony layer beneath. In the thickened belt of cartilage there is an enormous proliferation of cartilage cells, some of which have a regular arrangement, but by far the greater number are grouped without any attempt at arrangement, either as regards columns or size, and in many cases there is comparatively little matrix. Examine one of the small yellow points, and note that it is opaque. A process of calcification is in fact going on both in the matrix and in the cells. The patches of calcified cartilage are not arranged regularly, but crop up indiscriminately throughout the cartilage. In the same way blood-vessels make their appearance at irregular intervals in the cartilage, and, closely following them, appear spaces similar to those met with in ordinary bone, many of which are lined by a regular layer of pink cells or osteoblasts, and true bone, or a structure which very closely resembles it, is thus formed. Even in the midst of the bone formed in this position masses of the irregular cartilage cells may be seen.

Under the high power (× 300) the above appearances must be observed more closely, the great irregularity in the size of the cells,

in the matrix, and in the calcification of the matrix, the calcification of the cartilage cells at certain points, and at others the proliferation of these cells and an apparent transformation into osteoblasts. Even where true bone is formed, it appears to be laid down without any attempt at order or regularity, and bone, calcified cartilage, and true cartilage are mixed up apparently indiscriminately. The chief points to be noted are the enormous and irregular increase of cartilage, with irregular and deficient bone formation.

Examine under the low power (× 50) the piece of the shaft with its attached periosteum. Under the fibrous layer of the periosteum there is an enormous increase in the number of small round cells or osteoblasts, which now form a thick deeply stained layer. In the deeper part of this cellular mass a few trabeculæ, partly fibrous (stained pink), and partly calcified (stained green), may be seen. These trabeculæ form an open network, and they are seldom or never perfectly ossified ; they are rather calcified fibrous matrix. Beneath this osteoid tissue (very like that seen in an osteoid sarcoma—see section on Tumours) comes the true bone, somewhat loose in texture and irregular in structure, in some cases almost like spongy bone. In this tissue the number of vessels and osteoblasts is always very great, but the absorption cells are not markedly increased in number.

Under the high power (× 300) the pink round cells, or osteoblasts, running along with the numerous blood-vessels, are readily seen, not only beneath the fibrous layer, but between the granular looking trabeculæ, and in the spaces between the osseous trabeculæ. In normal bone these osteoblasts grow slowly, and form around them periplasts, which become gradually calcified, and bone is formed. In the case of rickets, however, these osteoblasts are formed in very large numbers, but any periplast which they may form, always small in quantity, is only imperfectly calcified : hence the above appearances.

The thickening of the ends of ribs at their points of junction with the costal cartilages gives rise to a peculiar series of knobs running down on each side of the sternum,—the so-called rosary. External to the rosary is a groove, due to the retraction of the less resistant ribs during the inspiratory effort, in consequence of which, too, the softened ribs are flattened or drawn in, and the sternum is more prominent.

In the flattened bones, such as those of the skull, a process similar to that under the periosteum of a long bone is met with ; but where the weight of the brain presses upon the soft tissue, the bone does not develop, and the skull at that point (occipital or parietal bone) remains very thin. The pelvis also is deformed in this condition, and curvature of the spine is often met with as a result of the softening and mal-development of the vertebræ.

From the above description of the process, it may be readily imagined that at the end of the developmental period, or where the disease gives way to treatment, the bones, when ossification sets in, may become very strong from the fact that the osteoblasts, &c. are present in such large numbers. This is found to be the case. The bones may be stunted and deformed, but they are often of enormous thickness and strength ; there ensues a condition of osteo-sclerosis, which is merely a thickening of bone due to an increase in the number of osteoblasts, with a corresponding laying down of true dense bony matrix.

Rarefying Ostitis.

230. Rarefying ostitis must be looked upon as a process rather than as a distinct disease, since it occurs in a great variety of conditions, where the apparent results differ widely. It is almost invariably met with as a result of injury to the bone after amputation, in absorption of the vertebræ by pressure of aneurisms, &c., or as a general condition known as osteo-porosis. In such a case, whether the condition be general or local, the following are the naked eye characteristics on making a longitudinal section through the diseased structures. The periosteum is frequently thickened and fleshy in appearance, and may be highly vascular. In the periosteal layer the formation of bone often takes place with great regularity, though this is not always the case. The layer of dense bone may have become very thin in such cases, and the porous bone is very rapidly reached. The trabeculæ of the spongy bone are considerably diminished in thickness, so that the tissue is open and friable, and in the spaces the medulla is present in very large quantities. The medulla is reddish and gelatinous, and on microscopic examination of a scraping is found to contain large

numbers of osteoclasts, or giant cells, and frequently numerous globules of fat, but comparatively few osteoblasts.

Prepare a piece of the porous bone, taken from a stump, in chromic and nitric acid fluid (§ 63, p. 46), cut sections (§ 67, p. 48), stain in picro-carmine (§ 73, p. 53), and mount in Farrant's solution (§ 98, p. 71).

On examination of such a piece of bone under a low power (× 50), the appearances are much as follows :—Near the free extremity of the bone the Haversian canals are undergoing great enlargement.



FIG. 87.—Rarefying ostitis. Portion of a vertical section of the first phalanx of the middle finger after amputation. (× 30.)

a. Haversian canals undergoing enlargement.
b. Free distal extremity of bone, with irregular surface and fine projecting spicules.
c. Periosteum.
d. Newly formed periosteal bone.

and their walls are ragged and irregular. This enlargement is most marked at the extreme end of the bone, at which point the trabeculæ project as fine spicules, and the spaces open one into the other. Lining these large spaces small pink dots may be seen, some considerably larger than others; these pink dots, as will be seen under the high power, are respectively the osteoblasts and the osteoclasts.

Whilst all these changes are visible in the bone itself, there is a superficial formation of bone from the deep layer of the periosteum.

The fibrous and vascular periosteum is readily seen near the surface from which blood-vessels may be seen dipping down into the newly formed bone, and running in between the trabeculæ. Accompanying the vessels are numerous pink dots, which will afterwards be recognised as cells, along with which are a number of fat corpuscles, and lying on the trabeculæ is a regular layer of osteoblasts.

Under the high power (× 300) examine first the periosteum, in the deeper layer of which there is almost invariably a new formation of bone, even in the most marked cases of rarefying ostitis. Note the pink or fibrous periosteum. Beneath this observe the greater vascularity, and the small vessels passing in between the bony trabeculæ, accompanied by a number of small round cells.

Lying on the trabeculæ are numerous deeply stained rounded cells,



FIG. 88.—Rarefying ostitis. Section of bone stained with picro-carmine. (× 250.)
a. Howship's fóvcolæ,
b. in which are lying giant cells or osteoclasts.
c. Hyaline border, due to oblique direction in which the section is made.

which appear to be partially imbedded in a layer of pink tissue. These are the osteoblasts lying on the most recently developed bony matrix. In this region the giant cells, or osteoclasts, are rare. Passing further inwards to the rarefied bone, observe the following appearances:—The Haversian canals are much enlarged, and at the same time are very irregular, the irregularity being due to a process of excavation, extending from the main cavity down into the bone of the surrounding Haversian system. These cavities, whether shallow or of

considerable depth, usually contain a number of small round cells; but, in addition, especially where the excavation is going on rapidly, and where it is far advanced, there are numerous osteoclasts, which lie in cup-shaped depressions all along the line of erosion. The cup-shaped depressions appear to be invariably associated with the absorption of bone, and are spoken of as Howship's foveolæ. The osteoclasts may be very large, may contain many nuclei, and are in all respects similar to the giant cell in the myeloid sarcoma. The

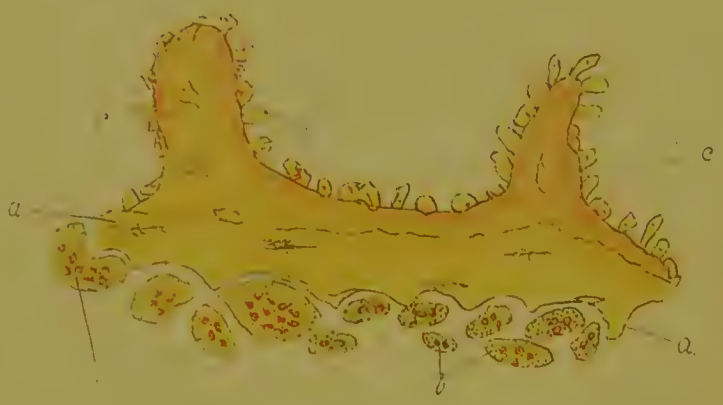


FIG. 89.—Simultaneous destruction and new formation of bone in a piece of bone found in a malignant epulis. Stained with picro-carmine. (× 250.)

a. Older bone, with
b. Osteoclasts in Howship's foveolæ.
c. Newer bone, with
d. Osteoblasts.

cells and spaces in rarefying ostitis are much more numerous than they are in a normal bone, where also they are always associated with a certain amount of absorption. In the pathological condition, however, the striped margin which is seen in the giant cell of the normal bone is very frequently absent. In the immediate neighbourhood of the giant cell it will be often found that the lime salts are removed before any other parts of the tissue.

In rarefying ostitis there is increased absorption of bone, unaccompanied by a corresponding new formation; but it must be remembered that new formation of bone invariably goes on to a certain extent in the deep or vascular layer of the periosteum, and that after the rarefying process has continued for some time the formative process may again predominate, and an osteo-sclerosis be the result.

In a section of malignant epulis, treated as directed for the porous bone, and examined under the high power, the two processes may be seen going on simultaneously. (See Fig. 89.)

Tubercular Caries of Bone.

231. This form of caries may be looked upon as a rarefying ostitis, accompanied by the formation of tubercle, which rapidly goes on to caseation. In its essential details the process is similar to tubercular ulceration of the lung. It is found most frequently in the spongy bones, especially in the vertebræ, the ends of the long bones, and in the os calcis.

If one of the vertebræ in which there is this condition be examined, it may be found to be diseased in the whole extent of the body; and the disease may be traced into the vertebræ above and below, passing entirely through the intervertebral discs. Where the disease is far advanced, there is simply a mass of soft caseous or putty-like material, which may be scooped away with the handle of a knife. Surrounding this softened mass is a quantity of grey or pink gelatinous material, which gradually extends into the bony tissue as an increasingly red granulation tissue, and fills up the spaces between the thinned trabeculæ. In consequence of the softening and absorption the bones may be very much deformed; they give way to external pressure, as in the vertebræ, where the weight of the upper part of the spinal column causes a crushing of the vertebral bodies, and a curvature is the result.

Treat with the chromic and nitric acid fluid (§ 63, p. 46). Be careful to avoid picric acid, as, if it is intended to look for tubercle bacilli, the picric acid adds much to the difficulties, whilst the other fluid does not interfere with the bacilli to any great extent.

Examine a section under a low power (× 50), and notice that as the healthy bone is left the medullary spaces become larger and more vascular, and that the giant cells are more numerous along the margins of the trabeculæ. In place of the fat cells of the medulla, a mass of granulation tissue is seen, gradually filling the somewhat enlarged Haversian spaces. It is composed principally of small round cells, and is traversed by a number of vessels. In the

mass of granulation tissue are small tubercle follicles, either single or in groups, with their giant cells and regular structure. (See Tubercle of the Liver, § 123, p. 115.) This tissue corresponds to the area of gelatinous looking tissue seen with the naked eye. Where caseation is complete, the bone has entirely disappeared, or is represented by small detached fragments or spicules, between which are granular shrivelled cells, droplets of fat (brought out by treating with osmic acid, § 80, p. 62); in fact, simply a mass of caseous *débris*.

Under the high power (× 300) the structure appears to be only a rarefying ostitis, in which the enlarged medullary spaces are filled with granulation tissue (masses of small round cells traversed by blood-vessels). In the latter tubercle follicles are developed, after which the whole undergoes caseation, as is the tendency in all tubercle formation. Near the centre of the caseous mass the absorption of the trabeculæ is complete.

Tumours of Bone.

232. The principal tumours of bone are *exostoses*, *osteoid chondroma*, *fibroma*, *myxoma*, *cystic tumours*, especially in the jaws; *sarcomas* of various forms, more especially the myeloid or giant celled sarcoma and the mixed sarcoma found in the lower jaw, as one of the most frequent forms of malignant epulis: osteoid and osteo sarcoma. *Primary cancer* is comparatively rare, but *secondary cancer* and *secondary epithelioma* are frequently met with, when they grow at the expense of the bone substance proper, so that the bone eventually becomes very brittle or fragile.

Chronic Articular Rheumatism, or "Arthritis Deformans."

233. On examination of a joint from a case of arthritis deformans the following appearances may usually be observed. At the point where there is the greatest friction the cartilage has frequently disappeared, and there remains simply a layer of dense polished bone; around this layer a ring of cartilage is often present, the articular surface of which is peculiarly soft and velvety to touch, and on examination with a

magnifying glass this is seen to be due to the presence of a number of villous processes. Passing further outwards to where the synovial membrane is situated, small nodules make their appearance, evidently the result of proliferation of the cartilage cells. These nodules in some cases assume a considerable size, but they give way as the ulceration spreads outwards. Around the joint itself, and in the synovial fringes, which become enlarged and more numerous, a process of ossification goes on in the periosteum, tendons, and muscles, in the latter stages of the disease, so that the joint is surrounded by a number of smooth dense bony masses, which are very characteristic of this condition.

Prepare a piece of the cartilage from such a specimen (early stage) in picric acid (§ 62, p. 46), stain with picro-carmine (§ 73, p. 53), and mount in Farrant's solution (§ 98, p. 71).

Examine near the margin of the ulcer under a low power (× 50). It will at once be seen that at some parts there is proliferation of the cartilage cells taking place, and that the cartilage cells within an enlarged capsule are well formed and of considerable size, but that those near the margin of the ulcer are very granular. It will be noticed, too, that there is an entire absence of the horizontal layers of cartilage cells, which have apparently been removed by friction. Between the vertical rows of cells near the surface of the bone (in which rows the proliferation above referred to takes place) some of the tissues have disappeared, so that a number of villous processes, already seen with the hand-glass, can now be further examined. Nearer the outer margin of the ulcer the process of cell proliferation is more marked, but the horizontal rows take more and more part in the process.

Under the high power (× 300), observe the granular cells, which are evidently fattily degenerated cartilage cells ; note also the well formed proliferated cells, and the splitting up of the cartilage into villous processes. The matrix between the rows of cells is under this power seen to be finely fibrillated, the fibrillation running down towards the bone. The villous layer consists simply of the deeper or vertical rows of cartilage cells, with a fibrillated matrix, the horizontal layers having been removed by the rubbing together of the two rough surfaces, the cartilage in this process playing merely a passive part.

The bone beneath the cartilage, as well as that formed around the joint, is very dense and smooth, and is the result of a chronic form of ostitis.

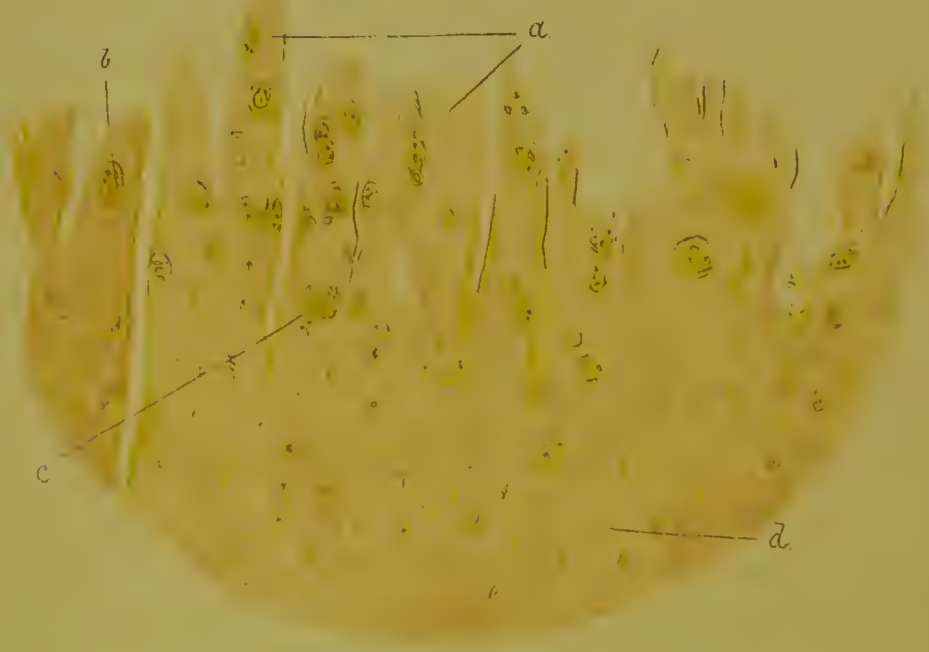


FIG. 90.—Section of ulcer of cartilage from a case of arthritis deformans. Stained with picro-carmine. (×80.)

a. Columns of cartilage cells, with accompanying matrix, from between which some of the matrix has been removed, after undergoing softening. (The velvet pile.)
b. Cartilage cells near the surface, fatty and granular.
c. Proliferating cartilage cells.
d. The deeper and more normal layer of cartilage.

In more *acute inflammation of cartilage*, the cells formed in the capsules are much more numerous, but are not nearly so large, whilst the matrix may gradually disappear altogether as the disease advances.

"TUMOR ALBUS," OR TUBERCULAR ARTHRITIS.

234. Tubercular arthritis is most frequently met with in delicate children after the age of three years, and is characterised by very marked clinical features. The pathological appearances are also very distinctive, and may be briefly described as follows. Where the disease is somewhat advanced, the serous or synovial membrane is

increased in thickness; it is soft and œdematous, and in many cases exuberant red granulations are seen projecting from the general swollen mass. This outgrowth passes along and around the margins of the cartilages of the joint, slowly detaching them from their bony beds. At the same time the granulations pass into the cartilage, gradually pitting it, and in the long run absorbing the cartilaginous material; it also passes into the articular end of the bone, giving rise to a condition exactly like that already described as rarefying ostitis, with tubercle. Along with these changes in the joint, the tissues surrounding the joint become soft and œdematous, and frequently appear as a mass of slightly pink gelatinous material, held in position only by the skin. In this disease it will at once be seen that the change commences on the serous or synovial membrane, in which there is a formation of vascular granulation tissue, which gradually invades the surrounding structures. In the granulations, as will afterwards be found, tubercle follicles, with caseation and suppuration, make their appearance. There is in fact a condition which may be compared with tubercular pleurisy, as tubercular disease of the bone may be compared with tuberculosis of the lung.

Take a piece of the joint, comprising synovial membrane, in its fungating condition, a piece of the cartilage, and a thin layer of bone from beneath the cartilage; prepare in chromic and nitric acid fluid (§ 63, p. 46), cut sections (§ 67, p. 48), stain with picro-carmine (§ 73, p. 53), and mount in Farrant's solution (§ 98, p. 71). Harden a second piece of the granulation tissue in absolute alcohol (§ 51, p. 42), cut sections, and stain for tubercle bacilli (§ 200, p. 283).

Examine under a low power (× 50), and observe that the granulation tissue consists principally of small round cells, through the mass of which a number of blood-vessels are ramifying, whilst in it there are also numerous tubercle follicles, which are especially well developed, and have the structure of tubercle follicles in any other tissue. Passing from the under surface of the granulation mass are small processes which may be seen to run into the substance of the cartilage, which is gradually being absorbed. In the cartilage itself the matrix appears to be diminished in quantity, whilst there is considerable proliferation of the cells within their capsules, or the small round cells resulting from proliferation are contained within no

definite capsule. The central part of the cartilage is least affected, but as the bone is again approached the process is repeated, until between the bone and cartilage there is found another mass of granulation tissue, which extends not only upwards into the cartilage, but downwards into the bone. In the bone all the appearances described under the heading of tubercle in bone are met with—rarefying ostitis, &c. It must be remembered, too, that tubercle commencing in bone may give rise to tubercular granulations under the cartilage, absorption of the cartilage, and ulceration into the joint, in which case there is also a form of white swelling. In the tissues around the joint in both cases similar tubercular granulations are found. In the tubercular masses tubercle bacilli may be found on examination under a high power.

Under the high power (× 300) all the above appearances should be confirmed—the encroaching of the granulation tissue on the cartilage, the proliferation of the cartilage cells, and the gradual disappearance of the capsules and the matrix. Then examine more carefully the structure of the tubercle follicles, the appearance of the granulations in the rarefying bone, and the commencing points of caseation, which can almost invariably be distinguished in these specimens. Examine a few of the muscular fibres from near the affected joint, and note that they are undergoing fatty degeneration, and that in some cases this is succeeded by great atrophy of the muscular substance.

In some forms of this disease it will be found that the cartilage cells, after proliferation, undergo rapid fatty degeneration, and are then, along with the softened matrix, absorbed.—(Billroth.)

Gouty Infiltration of Joints.

235. Whilst joints are under consideration, it is necessary to mention infiltration of the articular cartilages with urate of sodium, chiefly mixed with other urates, carbonates, and phosphates. These, when the infiltration is complete, form a chalk-like covering to the joint, or where the deposit takes place in the surrounding ligamentous and soft tissues, chalk-like masses are found, which may project through the skin. These so-called chalk-stones may give rise

to considerable inflammation, either of an acute or chronic form. When such a joint is cut into, soft chalky masses are first exposed, and the surfaces of the joint itself are found to be white, smooth, and chalky, from the rubbing together of the two surfaces.

On examination of a piece of the cartilage where the change is not so far advanced, in fresh condition (§ 37, p. 33), and under a high power (× 300), a number of acicular crystals may be seen arranged in stellate groups, the centre of each group being a cartilage capsule. The crystals are so arranged around this that the whole mass is like a thorn apple in appearance.—(Cornil and Ranvier). The distribution of the urates differs considerably in different cases, and it is held by some that the chalky deposits commence in the centre of the cartilage and then pass outwards, whilst others hold that they are most numerous near the surface, and that they gradually spread downwards to the bone.

Here, as in most of the diseased conditions of cartilage that have been examined, the altered cartilage plays a comparatively passive part in the process. As the infiltration takes place the mass is rubbed down by simple friction, as in fatty degeneration of the cartilage cells, where the cartilage matrix is softened or becomes fibrillated, and is triturated down; or in acute inflammation of cartilage, where the cells proliferate, the matrix softens and is removed, and the cartilage disappears. The more active the cells are, the greater is the divergence from the ordinary type of cartilage.

Primary tumours which grow in connection with joints.—These are very few in number, though secondary tumours, extending from bone or from the surrounding soft tissues, are by no means uncommon.

Of the primary tumours the most common are *ecchondroses*, which are found growing principally in the intervertebral discs; *fibromas*, forming the so-called loose cartilages of joints (knee); *lipomas*, rarely met with as arborescent growths from the fatty synovial fringes.

CHAPTER XI.

NERVOUS SYSTEM.

Tubercular Meningitis—Acute Hydrocephalus.

236. As it is impossible in a work of this character to give more than a very brief description of diseased processes of the nervous system, it will be advisable to enter somewhat more fully into a description of one or two only; the remainder may be left to the systematic text-book.

In tubercular meningitis there is a very good example of inflammation of the pia mater brought about by the tubercular deposit in the sheaths of the small vessels which ramify in that structure. It is very frequently the cause of death in children in whom there is general tuberculosis. In this condition the surface of the membrane is congested, whilst beneath it there is considerable flattening of the convolutions, owing to the distention of the ventricles (as will afterwards be seen), in consequence of which, too, the whole upper surface of the brain has a peculiar dry appearance, the fluid having been squeezed from the subarachnoid space. At the base of the brain, and extending along the fissure of Sylvius, along the superior crura cerebelli, and between the occipital lobes, the inflammatory process, with its accompaniment of tubercle, can be distinguished. In these positions the various soft structures are matted together by a slightly opaque yellowish lymph, and when this is torn away a quantity of turbid fluid, in which flakes of lymph are floating, exudes from the subarachnoid space. A similar fluid may be found distending the ventricular cavities, and the distention is especially well seen in the lateral ventricles. In most cases, when some of the parts near the base of the brain are separated, the small grey or white tubercle nodules may be seen to stand out prominently from the pink injected

pia mater. When a more careful examination of the pia matter is made between the tubercular points, it is seen to be thickened, somewhat cloudy, and covered by a thin yellowish, almost purulent, layer. Around the blood-vessels there is the same peculiar opacity, which, as will afterwards be found, is due to a small cell infiltration into the sheath of the vessel.

Cornil and Ranvier give such good directions for examining the pia mater for tubercle, that it is not necessary to apologise for introducing them here. "To find tubercle, the pia mater should be removed from those regions where it is most frequently found, such as the fissure of Sylvius and the superior crura cerebelli. The piece of the membrane should then be agitated in water till the adhering fragments of cerebral tissue are separated, and on holding it up to the light small whitish spots will be seen in the membrane. This examination must not, however, be considered sufficient. The pia mater should be carefully spread upon a glass slide, when, with a low power, granulations will be perceived which were not before recognisable with the naked eye."

Harden a piece of the pia mater with a piece of the brain tissue attached in Müller's fluid (§ 54, p. 43), stain a section in picro-carmine (§ 73, p. 53), and mount in Farrant's solution (§ 98, p. 71).

Under the low power (× 50) note first the general proliferation of cells, especially around the blood-vessels, and then examine one of the tubercular masses, which are situated most frequently near the points of bifurcation of the vessels (similar masses may be found at irregular intervals along the course of the smaller vessels, until they pass into the grey matter of the brain). Each of these tubercular masses consists of a number of cells, varying very greatly in size and shape. They accumulate around the vessel and distend the perivascular sheath. The vessel itself is frequently blocked by a coagulum at this point, and a peculiar process of endarteritis with a form of giant cell formation has been described as occurring in the vessel in the centre of the tubercle granulation.

Examine under the high power (× 300). Here the principal features to note are the large endothelioid cells which are found in the perivascular sheath. These vary in shape, and contain from one to four or more nuclei. Along with them are numerous small round

cells, each containing a single nucleus only. There is little or no reticular formation, and giant cells are entirely wanting. This structure, therefore, presents a very good example of rapidly growing tubercle.

Whilst on the subject of tubercle, it may be well to mention the chronic form which is sometimes found in the substance of the brain, but much more frequently in the cerebellum. This may commence in connection with the pia mater, but it rapidly extends into the substance of the brain. Take a typical mass from the cerebellum and examine it. It may be an inch or more in diameter. It projects from the surface, and also passes for a considerable distance into the grey matter. It is firm to the touch, and is somewhat tough on section. On examining a section the outlines are seen to be irregular and sinuous or lobulated, as though several tubercular masses had become fused. The centre of the mass is cheesy looking, and may be readily broken down with the fingers; but around the centre is a grey gelatinous zone, which gradually merges into the surrounding nerve tissue.

Harden a piece of such a tumour in absolute alcohol (§ 51, p. 42), stain a section with picro-carmine (§ 73, p. 53), and mount in Farrant's solution (§ 98, p. 71).

Examine under a low power (× 50), and observe the typical caseous structure in the centre, with a well-formed tubercular growth extending in all directions around. The tissue surrounding the tubercular masses is much more pink, and there may be seen a marked increase in the number of neuroglia cells. In the sheaths of the blood-vessels there is a process similar to that already described as occurring in acute tuberculosis, infiltration of the perivascular sheath with small cells, and obliteration of the lumen of the vessel.

All these appearances may be further verified under the high power (× 300), well-formed giant cells, fibrous capsule, and so on.

Apoplectic Cysts.

237. Fresh hæmorrhages, the result of rupture of single miliary aneurisms of a larger vessel, or a group of miliary dilatations, are so readily recognised that it is scarcely necessary to draw attention

to their ragged walls, and the dilatations on the vessels in the immediate neighbourhood. It may be well, however, to note the positions in which they most frequently occur. These are corpus striatum, optic thalamus, white substance of the convolutions, and more rarely in the pia mater, cerebellum, pons varolii, and medulla oblongata.

For changes in vessels see Aneurisms (§ 152, p. 167).

To examine the vessels around a hæmorrhagic focus open into it, and cut it away with the surrounding brain tissue. Macerate the whole carefully in water, changing the water every three or four days, until the brain substance is soft enough to be removed by small jets of water. When the vessels are thoroughly cleansed they may be spread out on a glass slide and examined. A small piece of the brain tissue with the vessels should be also hardened in Müller's fluid, and then in spirit (§ 52, p. 42), and examined in the ordinary way.

As a result of one of these hæmorrhages, there may be either a cyst or a cicatrix. Where a cyst is formed the walls are found to be tough and fibrous, whilst the contained fluid has usually a yellowish tinge. In the immediate neighbourhood of the fibrous wall there is a peculiar yellow opaque tissue.

Examine small scrapings from the inner wall under a high power, and observe that there are numerous small round cells which contain crystals, evidently derived from altered blood pigment. Similar larger free crystals may be seen, and also a number of granular cells (compound granular corpuscles), which, stained with osmic acid (§ 80, p. 62), give a black reaction. A number of fat globules are also usually met with in this position.

If a thin section of the wall be examined unstained, it will be found to consist in great part of neuroglia cells (Fig. 91), the processes of which are closely matted together, with here and there a few altered nerve fibres, many of which are varicose and fatty. Between these are crystals or granules of altered blood pigment. The crystals are more numerous in the opaque yellow zone surrounding the capsule, where the fatty granules are also more numerous. In the sheaths of the vessels fatty granules, altered coloured and colourless blood corpuscles are found, whilst in the larger cells, lining these spaces or lying free in them, blood crystals may frequently be seen. In a cyst formed as the result of an embolic softening no blood

crystals are found in the walls of the sac, as there has been *no great escape of blood from the vessels.* In embolic softening there is simply

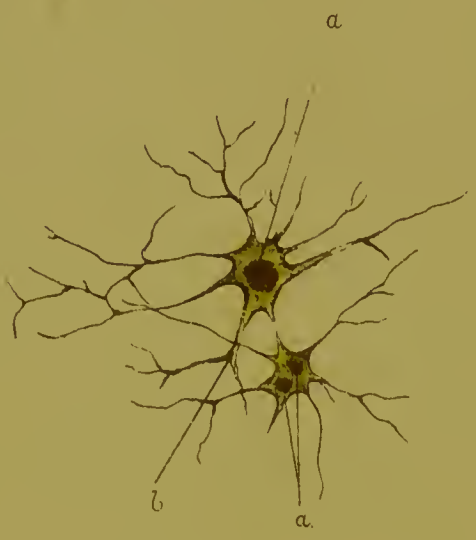


FIG. 91.—Drawing of connective tissue or Deiter's cells, from dense connective tissue of the wall of a cyst. Stained in carmine and half cleared up. (×600.)

a. Single or double nuclei.

b. Delicate branching processes.

a fatty degeneration of the tissues, and a mass of granular *débris*, fat crystals, &c. is all that is found under the microscope, except that there may be an increase in the number of leucocytes around the vessel, and other evidences of slight inflammatory changes. Where the softened area is due to thrombosis, in which the cutting off of the blood supply is gradual, there is a true fatty degeneration or yellow softening. The so-called red softening of the brain appears to be an inflammatory process leading to fatty degeneration, in which there is very marked congestion of the vessels. In such a condition there is proliferation of the neuroglia cells, exudation of leucocytes, hæmorrhages into the perivascular sheath, &c. In connection with the various degenerative changes which occur, the amount of blood in the part, the amount of infiltration with leucocytes, the extent and rapidity of the fatty change in the nerve fibres and connective tissue cells, must all be remembered when it is attempted to explain the causes of the yellow or the red forms of cerebral softening.

Changes in the Medulla Oblongata in Hystero-Epilepsy.

238. Section taken from a case in which the vessels at the base of the brain were healthy, but there was a large amount of subarachnoid effusion; the vessels of the dura mater were anæmic; and there was considerable subarachnoid serous effusion on the surface at the vertex. The fourth ventricle contained about a couple of drachms of clear fluid. In the floor of the fourth ventricle, and in the lateral ventricle, well-marked granulations, almost like grains of sand sprinkled over the ependyma, were found. The vessels in the optic thalami contained much blood, and were dilated, as were also those in the white substance of the cerebral hemisphere.

The medulla oblongata was somewhat firm, and had a greyish tinge in the region of the corpora olivaria; the vessels of the pia mater and those of the medulla itself were engorged. Harden a thin slice of the medulla oblongata in a mixture of Müller's fluid and spirit (§ 54, p. 43), Müller's fluid alone (§ 53, p. 42), or weak chromic acid (§ 57, p. 44), taking the slice from between the lower two-thirds of the fourth ventricle. Cut sections (§ 67, p. 48). Mount one section unstained in Farrant's solution (§ 98, p. 71), a second stained in picro-carmine (§ 73, p. 53), in Farrant's solution, and a third stained by Weigert's method, as follows:—Stain a section hardened in Müller's fluid, or bichromate of potash (§ 55, p. 44) for twenty-four hours in a concentrated watery solution of acid fuchsin (soda salt of rose aniline sulphate). Wash in water and transfer to an alkaline solution of alcohol, "viz., 100 c.c. of absolute alcohol with 10 c.c. of a solution made by dissolving 1 gramme of fused caustic potash in 100 c.c. of absolute alcohol, and filtering for a few seconds, until the first sign of the grey nerve tissue of the section becomes visible;" wash in water, "which must not be acid," and dehydrate with absolute alcohol saturated with sodic chloride, to preserve the colour of the section. Clear with oil of cloves, and mount in Canada balsam (§ 96, p. 69). In sections prepared in this manner the medullated nerve fibres stand out as brilliant red lines or points, even those in the anterior horns of the spinal cord. The sheath, or part of it, is stained by this method. "The ganglion cells and connective tissue (especially in sclerosis), with the pia mater, vary in tint from a pale appearance to

an exquisite blue, which latter is increased by putting the sections into a solution of one part of hydrochloric acid to five of water, and again into water before dehydrating them with alcohol. These tissues can also be stained blue by hæmatoxylin," "before or after colouring with the acid fuchsin." For the central nervous system, according to Weigert, this is invaluable, but for peripheral nerves it is of no use.

Another section may be stained in carmine, and then, instead of



FIG. 92.—Hystero-epilepsy. Section through the medulla oblongata, at the level of the hypoglossal nucleus, to show the granulations and the increase in the amount of connective tissue. (× 50.)

a. Central granulation.
b. Vessel with thickened walls.
c. Increased connective tissue pad.
d. Nucleus of hypoglossal nerve.
e. Longitudinal fibres of the medulla.
f. Transverse fibres.
r. Raphe.

being completely cleared up, it should be treated with methylated spirit (instead of absolute alcohol), and left in this long enough to

drive out only part of the water; clear up partly in clove oil, and mount in dammar mounting fluid, and examine at once, as preparations made in this way do not retain the characteristic appearances for any length of time. Such a method is especially useful for demonstrating the neuroglia cells with their delicate branching processes.

Examine this half cleared-up section under the low power (× 50). In the arachnoid and pia mater, the blood-vessels, especially the larger ones, are considerably distended, whilst in the smaller vessels there appears to be a peculiar brown pigmentation of the blood. The outer and middle coats of these vessels, even under this power, are seen to be somewhat thickened. In the pia mater and the connective tissue trabeculæ running from it into the nerve substance, there is a marked increase, evidenced by the large pink strands which run from the deep layer. In the medulla itself the vessels are distended with brown pigmented blood, their walls are thickened and pigmented, and around them are a number of pink bodies, evidently leucocytes. The whole section under this power has a much more pink appearance than a normal medulla, the pink tinge being due to the increase in the amount of fibrous tissue, which in this instance is most marked near the floor of the fourth ventricle. In the same position are a number of greatly distended vessels, closely resembling sinuses, and these at certain points have evidently given way. The nerve cells in this region are deeply pigmented. Growing into the fourth ventricle are the masses of granulation tissue above referred to. They are composed of masses of small round cells, which grow up beneath the epithelium of the ependyma, pushing the latter before it, or breaking through the epithelial layer, and continuing to grow for some time; eventually in either case they fall to one side, either to the floor of the ventricle or towards a similar granulation. In consequence of this, cavities lined with a layer of epithelium are frequently found near the base of these granulation masses. Running into the masses of granulation tissue, as a rule, small vessels may be seen very similar to the vessels in the floor of a granulating wound.

Under a high power (× 600) the following appearances may be noted:—Thickening of the adventitia, and, in a minor degree, of the muscular coat of the vessels. Around the dilated vessels are numerous wandering cells and connective tissue corpuscles apparently

in connection with the thickened adventitia. The nerve cells are deeply pigmented, the pigment being collected around the contractile



FIG. 93.—Drawing of connective tissue, &c. of medulla oblongata in case of hystero-epilepsy. Stained with carmine and half cleared up. (×800.)

a. Connective tissue nuclei, around which there is as yet no formed material. Contractile nucleus well marked.

b. Nucleus of wall of (*c.*) capillary vessel.

d.d[1]. Connective tissue corpuscles in different stages of development. (Deiter's cells.) Note the branching processes.

e. Nerve cells, with pigmented nuclei. Each contains a nucleolus.

f. Young connective tissue nuclei or leucocytes lying in lymph space.

nuclei. On examining the connective tissue the first thing that calls for notice is the great number of leucocytes as compared with a healthy section, and the second is that the Deiter's cells or neuroglia cells are also very much more numerous. Between the simple connective tissue nucleus, which has no formed material, and no protoplasmic investment, and those which have a great number of finely branched processes are cells in all the various stages of



FIG. 94.—Hystero-epilepsy. Section through central granulation (*a*.) of Fig. 92. (× 350.)

a. Granulation as before described.
b. Ciliated epithelial cells on floor of ventricle.
c. Cavity lined with epithelium.
d. Cavity from which a vessel has fallen.
e. Fibro-cellular connective tissue, passing from pad beneath to the granulation mass.

development. In some parts of the field the masses of contractile material are arranged in rows, or they may occur singly, when

frequently they are seen to be about to divide. They gradually take on additional structure, processes are sent out, which divide and subdivide until a dense network is formed. Where these cells occur in such great numbers they form a species of fibrous tissue, to which, in this disease, the increased hardness of the medulla is partially due. The hardness is also partly due, no doubt, to the distention of the various vascular channels.

The branching neuroglia cells precisely resemble those which will be afterwards described as occurring in glioma.

Under this power examine the granulations, and note that the cells of which they are composed are continuous with those deeper down in the pad of tissue which is found in the floor of the fourth ventricle. Then, too, notice that the epithelium in the enclosed cavities is similar to that which is found on the free ependymal surface, especially that which is seen to cover the bases of these granulations.

Examination of a Section from a Case of Epilepsy.

239. To the naked eye there was little or nothing abnormal in appearance in the medulla itself beyond slight congestion and increased firmness. Treat as for the last section (§ 238, p. 363), and examine under a low power (× 50). Near the margin of the section (taken from about the same level as in the last case, between the lower two-thirds of the fourth ventricle) the most prominent features are large gelatinous looking bodies, which are accumulated in large numbers along the lines of the pia mater and blood-vessels, especially wherever there has been an exudation of blood. In addition to these there are rounded, irregular bodies, which do not stain with iodine, and which are not nearly so numerous as the first-mentioned bodies. Note here that there is an increase in the amount of connective tissue, but that there are no granulations. The ependyma, however, is thrown into a series of folds, which are well supplied with blood. The epithelium is intact, and there is simply a slight exaggeration of the normal folding. The nerve cells are deeply pigmented, the vessels are engorged with blood, their walls are hypertrophied, and in some cases pigmented, and the perivascular spaces are distended.

Under the high power (× 300) note carefully the above conditions, as in the last section, then examine closely the two kinds of round bodies, since these occur in a great number of nerve diseases, and it is necessary to be able to distinguish one fromthe other. The amyloid bodies stained with iodine, and left for some time, give a

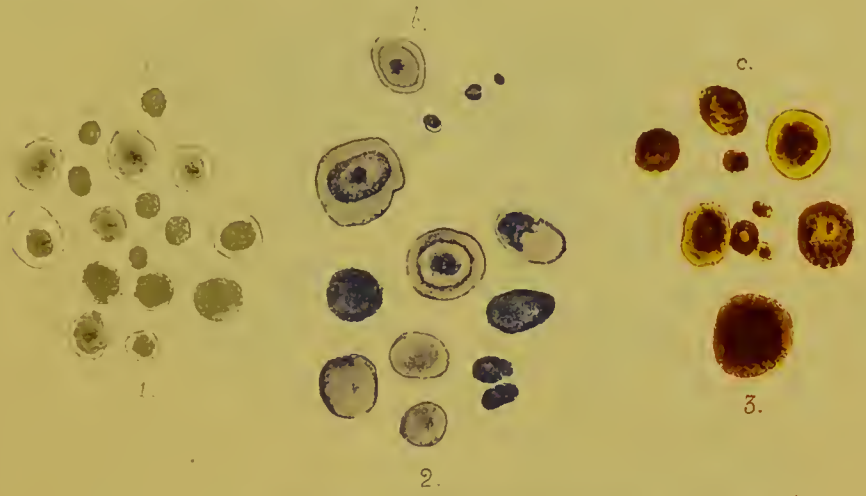


FIG. 95.—Amyloid bodies, &c. from epileptic medulla. (× 700.)
a. Stained with osmic acid.
b. Stained with iodine and sulphuric acid.
c. Stained with iodine.
Here the stages of development from the blood corpuscle to the amyloid body may be seen.

decidedly brown reaction. Some of them are surrounded by a yellow zone. The colloid bodies are simply stained yellow.

With picro-carmine the amyloid bodies do not stain so deeply as the colloid bodies. The amyloid bodies stain with logwood, also with iodine and sulphuric acid. Here the blue colour does not appear for some time, but after it once commences it gradually deepens until it becomes a deep indigo. Concentric circles may be seen if the cell is examined before the colour becomes too deep, in which the centre is always much darker than the periphery. In some of the amyloid bodies nuclei may still be discerned in the centre. At certain parts of the section the amyloid bodies are seen to be of *different sizes*, and they appear to be mixed indiscriminately with red, or perhaps white, blood corpuscles. Some are about the same size as the blood corpuscles, but are apparently undergoing various transformations, whilst others are much larger, and are fully developed amyloid bodies; the nucleus or dark part becomes granu-

lar, and the clear part more indistinct, after which the granular part becomes homogeneous, and is fused with the clear zone. In these



FIG. 96.—Amyloid bodies, &c. from epileptic medulla. Unstained. (× 700).

a. Normal blood corpuscles.
b. Swollen blood corpuscles.
c. Granular blood corpuscles.
d. Enlarged granular blood corpuscles.
e. Enlarged homogeneous corpuscle.
f.g. Amyloid bodies.

bodies there are apparently all transition stages from the red or white blood corpuscle, or connective tissue corpuscle, to the fully developed amyloid body, whilst the colloid body, as will be seen under the description of locomotor ataxia, is derived from the alteration of the axis cylinder of the nerve fibres in myelitis.

Degenerations of the Cord.

240. Before considering the degenerative lesions of the cord, it will be necessary to say a few words as to the tracts along which these lesions run. It may be taken as a general axiom that all degenerative changes run in the same direction as the impulse which travels along that tract in the normal condition. These directions will perhaps be best explained by the aid of a diagram of a section through the spinal cord at the cervical enlargement. In the various tracts an arrow is placed, with the point turned upwards in the tracts in which the degeneration ascends, and downwards where the degeneration descends. If the cord were injured throughout its whole extent—say by pressure at all points of its surface—a

secondary degeneration would be found passing upwards in the columns so marked, and downwards in the columns in which the

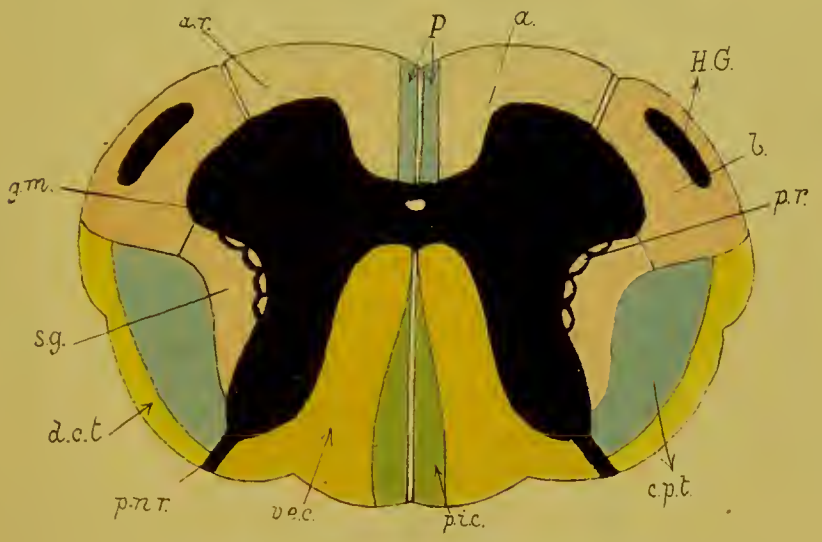


FIG. 97.—Diagram of the cord at the level of the cervical enlargement. Altered from Flechsig.

P. Direct pyramidal tracts.
a. Ground bundle of the anterior columns.
H.G. Haddon and Gower's supposed lateral sensory tract.
b. Mixed zone of the lateral columns.
a.r. Anterior nerve root, running from the anterior horn of grey matter.
p.r. Processus reticularis.
s.g. Limiting layer.
c.p.t. Crossed pyramidal tract.
d.c.t. Direct cerebellar tract.
p.n.r. Posterior nerve root running from the posterior horn of grey matter.
p.e.c. Postero-external column.
p.i.c. Postero-internal column.

Degenerations follow the course of the arrows in the several regions.

arrow points downwards. Not only is this the case, but there are certain lesions—locomotor ataxia for instance—in which the primary lesion is followed by an ascending degeneration; and, on the other hand, there are lesions in the motor area of the brain, such as hæmorrhage, softening, tumours, &c., which are invariably followed by descending degeneration—descending degeneration travelling in the direction of the motor impulse, whilst ascending degeneration travels in the direction of the sensory impulse, or from the periphery towards the centre.

Descending Degeneration.

241. In a case of descending degeneration, where the primary lesion is in the brain—in the corpus striatum, or in the hemispherical ganglia in the region of the fissure of Rolando—there will be descending degeneration first in the motor area (pyramid) of the same side, in the medulla oblongata. It is here quite out of the question to follow the lesion from the corpus striatum to the upper part of the cord. Below the point of decussation the lesion may generally be observed in two positions—*1st*, in the small strip which bounds the antero-median fissure—direct pyramidal tract; and *2d*, in the crossed pyramidal tract, situated in the postero-lateral part of the antero-lateral column, which does not come quite to the surface, as it is bounded externally by the direct cerebellar tract.

On examining a section of the cord in which this descending degeneration is well marked, the principal change is a peculiar firmness to the touch of the areas mentioned, whilst those areas also assume a much greyer and more gelatinous appearance than the corresponding areas on the opposite side. To prepare the cord, cut it into thin segments, from one-fourth to one-eighth of an inch in thickness, leaving them attached by the anterior band of pia and dura mater.

Harden in Müller's fluid (§ 53, p. 42), bichromate of potash (§ 55, p. 44), or Müller's fluid and spirit (§ 54, p. 43). When the process of hardening is not proceeding rapidly enough, bichromate of ammonia (§ 56, p. 44) may be used. Mount one section, unstained, in Farrant's solution (§ 98, p. 71); stain a second in carmine (§ 75, p. 58), and mount in Canada balsam (§ 96, p. 69). Another section should be mounted according to Weigert's method (§ 238, p. 363), and a fourth should be stained slowly with carmine (§ 75, p. 58), washed well in acidulated and then in pure water. Treat with a weak solution of osmic acid (§ 80, p. 62), after which it may be mounted in Farrant's solution, or half cleared up (§ 238, p. 364), and mounted in dammar varnish.

Hold the unstained section up to the light, and note that in the crossed pyramidal tract the tissue is much more transparent than the other white matter; it resembles much more nearly the grey matter

in appearance. This change is not so readily recognised in the direct pyramidal tract, which is very small, and in some cases is represented by a few fibres only.

Examine the carmine-stained specimen under a low power (× 50), and note that in the affected areas (the left direct and right crossed pyramidal tracts) the tissue is much more pink than is the normal nerve tissue. There appears to be a marked increase in the amount of neuroglia, with a corresponding diminution in the number or size of nerve fibrils.

Under the high power (× 300) the increase in the amount of neuroglia cells can be very readily discerned, especially in the carmine and osmic acid stained specimen. The myelin sheath of the nerve has disappeared, but the axis cylinder, deeply stained, can be easily distinguished. In this section it will be noticed that the affected area is not nearly so deeply stained by the osmic acid as is the part where the fatty myelin sheath is still present.

Examine a fresh section of a similar cord—or one in which the degeneration is not so far advanced, which is softer, and not so transparent—under a high power, and notice that in the affected area are numerous bodies about three times the size of a red blood corpuscle. Each of these contains two or three nuclei. Also observe the compound granular corpuscles; myelin drops, rounded or tadpole shaped; colloid masses, few in number, probably derived from the axis cylinders; and a few small moniliform fibres. None of these bodies are stained brown by iodine. In the perivascular sheaths fatty globules and granules can frequently be seen, especially in the specimens stained with carmine and osmic acid; but few of the above bodies can be made out in a hardened specimen of the cord. This is simply a secondary degenerative process of the nerve fibres, accompanied by a formation of neuroglia.

Locomotor Ataxia and Ascending Degeneration.

242. On examining the cord from a case of locomotor ataxia, the following points may be distinguished with the naked eye:—About the level of the sixth cervical vertebra—the dura mater and pia mater thickened—the posterior nerve roots are small and transparent, and

the posterior columns, in an advanced stage of the disease, such as that under examination, are grey and gelatinous looking; but the texture of this gelatinous mass is firm. The thickened pia mater is firmly adherent to the posterior columns.

Prepare the cord as for descending degeneration (§ 241, p. 372), or harden it in a ten per cent. solution of chloral hydrate. Change the fluid after twenty-four hours, again at the end of the third day, and at the end of the first, second, and fourth weeks; after which the cord may be left in the fluid until it is transferred to the gum and syrup solution, before the sections are made. Stain and mount sections as for descending degeneration (§ 241, p. 372), and in addition stain one in picro-carmine (§ 73, p. 53), and mount in Farrant's solution (§ 98, p. 71); make longitudinal sections, and treat in the same manner.

Examine a transverse section under a low power (× 50), and note that in the postero-external columns, immediately internal to the posterior roots, there is an increase of fibrous tissue or neuroglia. This increase is recognised from the fact that the carmine stain is taken on deeply, whilst with Weigert's method the tissue appears more blue, and with osmic acid the blackening is not nearly so marked as in the normal condition. When the change is confined to this region the disease is locomotor ataxia pure and simple. It will be found, however, that in most cases there is a secondary degenerative process which extends along the lines of the sensory tracts, and therefore passes upwards. This gives rise to an increased connective tissue formation, with corresponding changes in the nerve tubes, and these changes must be looked for in the inner parts of the postero-external columns, in the postero-median columns, and in the direct cerebellar tracts; whilst Haddon and Gower also describe an area opposite the outer angle of the anterior horn of grey matter, either at the surface in the dorsal region, or close to the surface at the level of the cervical enlargement. In all these areas there is a new formation of fibrous tissue which takes on the pink stain very deeply. Scattered at irregular intervals through this are more opaque patches, which are collections of breaking down axis cylinders or colloid bodies derived from swollen axis cylinders. Near the surface the vessels are considerably congested, whilst their walls are also thickened.

Where the disease is furthest advanced, *i.e.*, in some parts of the postero-external columns, the axis cylinders have disappeared altogether.

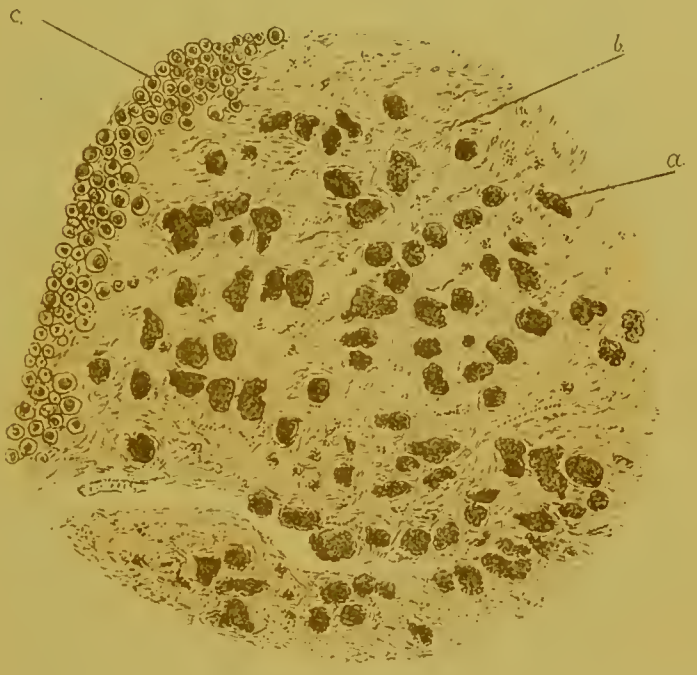


FIG. 98.—Locomotor ataxia. Small portion of nerve tissue from the direct cerebellar tract. Stained with carmine. (× 120.)

a. Compound granular corpuscles and colloid bodies.
b. Newly formed fibro-cellular tissue (pink).
c. Healthy nerve fibres.

Examine under the high power (× 300). Note first the condition of the distended vessels. In the perivascular sheath there is a considerable quantity of fat present in the form of granules and globules, which are readily stained by osmic acid. Around the distended blood-vessels leucocytes may be seen. This loading of the connective tissue with wandering cells is seen also in the pia mater, in which position, too, the perivascular spaces are filled with fatty particles, and in some instances there is a substance giving, with osmic acid, a black reaction in the vessel itself.

In longitudinal and transverse sections, examine the nerves of the affected areas. In these there are very marked changes, such as may be found in most cases of myelitis. First a number of constrictions may be seen at intervals (in the longitudinal section) along the axis cylinder, the myelin remaining intact, or but slightly affected.

Later, the alternate constriction and swelling are more pronounced, and the varicosity is very marked. At other points the swollen masses

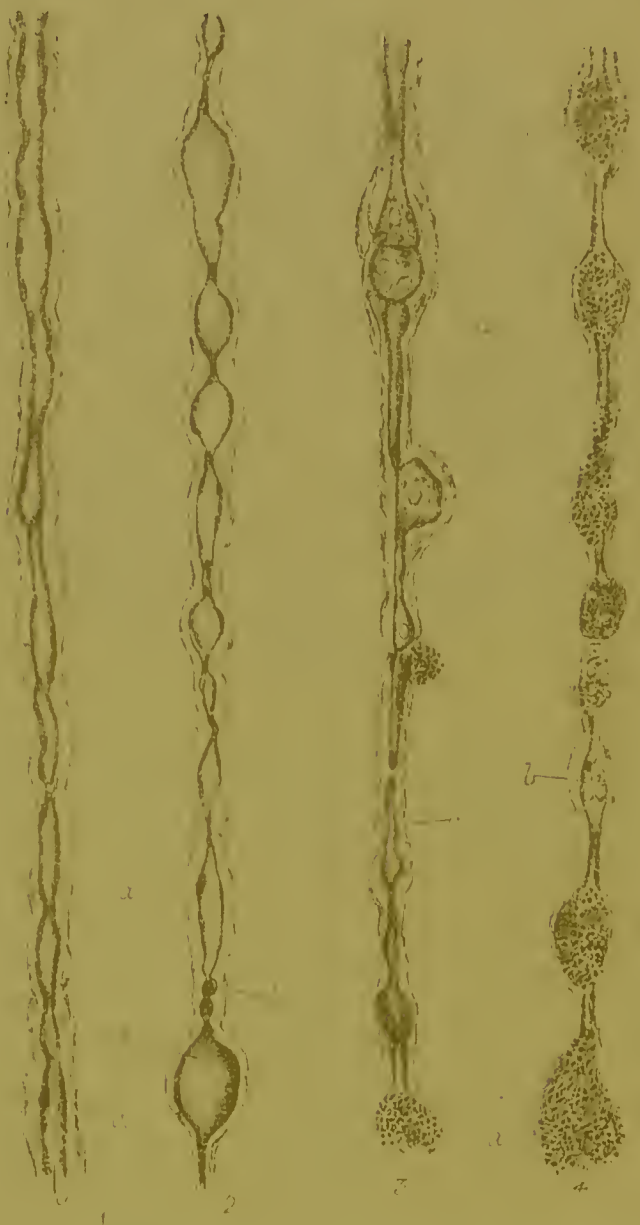


FIG. 99.—Locomotor ataxia. Nerves in various stages of degeneration, from the postero-external columns in the cervical region of the cord. Stained with osmic acid. (× 400.)

a. Axis cylinders become more and more swollen and constricted, and then undergo fatty degeneration.

b. Nerve sheath, which gradually loses its distinct ontline.

of axis cylinder are seen to be vacuolated or nucleated, and in other parts they form the granular masses seen scattered throughout the

fibrous tissue.—(See Fig. 98.) Where these are seen in a transverse section of the cord, or where the disease is not very far advanced, the large colloid bodies are very readily recognised from their clear

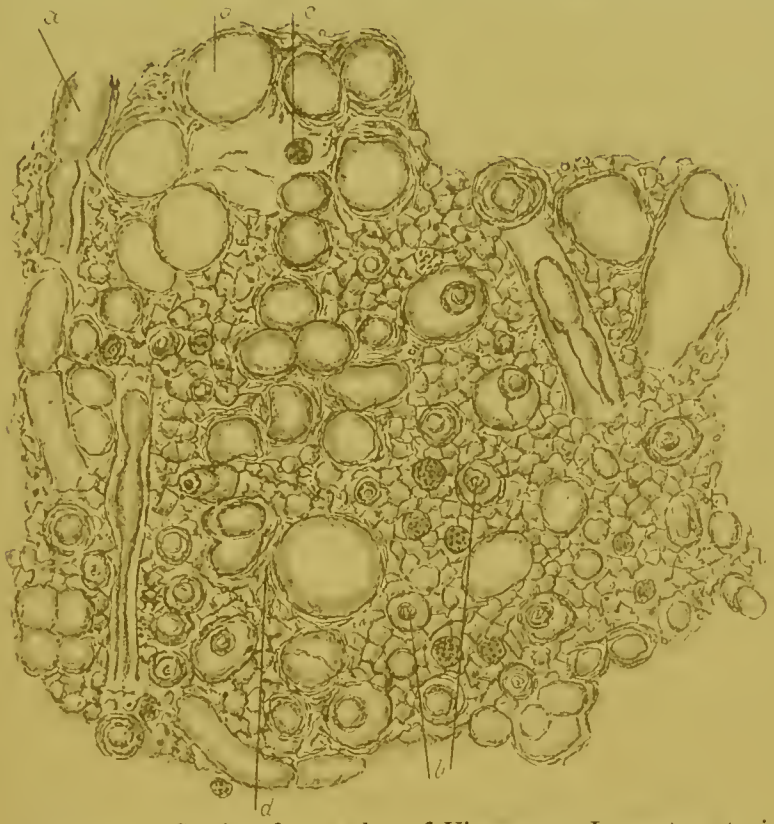


FIG. 100.—Section from valve of Vieussens. Locomtor ataxia. Unstained. (700.)

a. Enlarged and colloid axis cylinder.
b. Sheath in process of breaking up.
c. Connective tissue nucleus.
d. Sheath almost disappeared.

homogeneous appearance, and often from their size,—for it must be remembered that there is not so great a difference in size between the colloid and amyloid bodies as is sometimes stated.

In the above condition be careful to distinguish between the area of the primary disease, postero-external columns, and those which are affected by a secondary ascending degeneration, postero-median, direct cerebellar, and Haddon and Gower's tracts, which may be affected *above the point of primary lesion* as the result of any injury to the cord.

In examining this cord, a careful search should be made for altered conditions in the posterior horn of grey matter, pigmentation,

or swelling of the nerve cells, and also for similar conditions in the anterior horn.

Varicose swelling of the axis cylinder and hyaline thickening of the sheath, with increase in the neuroglia and colloid bodies, may also be found in the following positions in well-marked cases of locomotor ataxia; optic tracts and nerves, auditory nerve, and striæ acousticæ, fifth nerve, fourth nerves, at their decussation in the valve of Vieussens, corpora quadrigemina in the roof of the aqueduct of Sylvius, hypoglossal nerves, &c.

Waxy Disease of the Cord.

243. Waxy degeneration of certain elements of the cord is comparatively rare, but it must be mentioned. Prepare as for descending degeneration (§ 241, p. 372), stain a section in methylaniline violet (§ 76, p. 59), and mount in Farrant's solution (§ 98, p. 71). Notice first the affection of the middle coat of the vessels, then the degeneration not only of the connective tissue fibres, which are swollen and red violet in colour, but also of the ganglion cells, the processes of which become red violet and swollen, whilst the body of the cells also takes on the red violet stain. Pigmentation of the large multipolar cells is frequently met with, also vacuolation of the cell. In pigmentation there is an accumulation of brown granules around the nucleus, whilst in vacuolation the nucleus can usually be observed, though it is most frequently displaced to one side of the cell. As a result of inflammatory changes of the grey matter of the anterior horn, the cells may have become extremely small and atrophied, in which case the horn itself is much smaller than normal, and the amount of fibrous tissue is considerably increased. For other diseases of the cord the student is referred to systematic works on Pathology and Medicine.

Tumours growing in connection with the Membranes of the Brain and Cord.

244. *Syphilitic gummata* occur in the dura mater, and in the pia mater also, in the brain substance, especially towards the base of the

brain. *Fibroma*, *psammoma*, *lipoma*, *glioma*, *osteoma*, *myxoma* (frequently with cyst formation), *myxosarcoma*, *sarcoma* — melanotic, spindle-celled, and small round-celled—(usually met with as a primary growth in children) occur. *Carcinoma* is almost invariably secondary *Parasites—Cysticercus cellulosæ* and hydatid cyst. In addition to the above—which, with the exception of the glioma, occur in both brain and membranes—*chondroma* is also found growing in the meninges. Dermoid cysts are described as occurring in the brain and dura mater.

Retina.

245. To harden the retina for examination, use Müller's fluid (§ 53, p. 42). If the whole eye can be obtained, place it intact in the hardening fluid, or make a few minute punctures in front of the attachment of the cornea. Allow the tissues to harden, and then treat as for nerve tissues. If the posterior half of the eye only can be obtained—as is usually the case, especially when specimens are taken from private patients—before placing in the hardening fluid turn the tissues inside out, *i.e.*, have the retina on the convex instead of the concave surface. In this way it is kept tense, and much better preparations will be obtained. In place of Müller's fluid, a ten per cent. solution of chloral hydrate may be used in the same way.

The peripheral nerves are to be treated in the same way as pieces of spinal cord (§ 241, p. 372).

CHAPTER XII.

TUMOURS.

246. It is unnecessary to enter into definitions and classifications of tumours. These growths may, for the sake of convenience, be considered in three large groups, which may be taken in the following order :—

I. Simple or histioid tumours, composed of tissues which deviate but slightly, if at all, from the tissues of which a healthy body is built up. These tumours are mesoblastic in their origin, and consequently are mainly composed of some form of connective tissue.

II. Sarcomatous tumours, composed of tissues more or less embryonic in type, in which there may be some attempt at higher development—which attempt, however, is always abortive. These are also mesoblastic, and are therefore composed of young connective tissues.

III. Cancerous tumours, in which some or all of the tissue elements may be present "in excessive or erratic forms." There is a loss of balance between the tissues, which may be derived from mesoblast and hypoblast or epiblast.

Simple or Histioid Tumours.

247. Before the description of the individual tumours of this group is commenced, it may assist the student very materially if a few general characters of this group be given.

All simple tumours grow comparatively slowly. They are single or simple, rounded or lobulated, and usually are surrounded by a fibrous capsule. They are non-malignant, and give rise to no incon-

venience or injury, except by their weight and mechanical pressure. The capsule by which they are surrounded is, like the pseudo-cyst of the hydatid cyst, formed by a chronic local inflammation and connective tissue formation, set up by the presence of the tumour itself. They are liable to certain degenerative processes, of which fatty degeneration and calcification, ulceration, colloid or mucoid degeneration—colloid of the cells, mucoid of the fibrous or connective tissue—are the most important. Hæmorrhages are also frequently met with in the softer forms, and inflammatory changes may be set up by mechanical injury or by the action of irritant substances. On making a section into a lobulated tumour of this class, fibrous bands, along which the larger blood-vessels run, are seen passing in from the capsule, between the individual lobules.

Myxoma.

248. This tumour is non-malignant, though it is composed of a tissue which is in many respects embryonic, as it is found only in the vitreous humour in the adult. It is met with in fœtal life as the subcutaneous tissue, from which fatty tissue is later developed. Whaton's jelly is similar in structure, as is also young fibrous tissue. Myxomatous degeneration of the villi of the chorion is spoken of as a form of multiple myxoma. In this case there are rounded or pear-shaped masses of myxomatous tissue, held together by portions of the healthy villi. Myxomas are also found as nasal polypi in the submucous tissue, in subcutaneous tissue (case described from subcutaneous tissue of the breast), in the intermuscular septa, in the connective tissue, between the bundles of nerves, in periosteum, and in subserous fat. In rare cases they are met with growing on the umbilical cord.

These tumours do not often reach any very great size; but in rare cases they may be very large. They are lobulated, and are surrounded by a delicate capsule, from which trabeculæ run in. The tissue between the trabeculæ is clear and gelatinous looking, and is often compared in appearance to a mass of boiled tapioca. Running along the trabeculæ, and into the gelatinous substance, are small blood-vessels, seen as thin red lines. Usually these have given

way, as the mucous tissue does not afford them much support; so that small hæmorrhages, red, brown, or yellow, acording to their age, may be seen in the clear mass. If a fresh section be made, the gelatinous material projects beyond the firmer trabeculæ. Take a scraping from this surface, and note that it is a somewhat viscid fluid, which, if examined under the high power, is found to contain a number of coloured blood corpuscles, and some nucleated cells, with one or two nuclei and branching processes. Unless these are stained, it is very difficult to distinguish them. Take a small piece of the tumour and immerse it in acetic acid or alcohol, and it immediately becomes opaque from the precipitation of the mucin which lies between the branching cells.

Harden a piece of the tumour in Müller's fluid and spirit (§ 54, p. 43), cut sections (§ 67, p. 48), stain with picro-carmine (§ 73, p. 53), and mount in Farrant's solution.

Examine under the low power (× 50), and note that in the subcutaneous tissue are trabeculæ, which in this instance are composed of very cellular material, but which in most cases are more fibrous. Along these bands may be seen running small blood-vessels. In the compartments formed between these bands is the true myxomatous tissue. It is made up of a number of branching cells, each having one or more nuclei deeply stained. There is a large quantity of protoplasm around the nuclei, and between the individual cells are spaces which, in the fresh condition, are occupied by mucin. The mucin, in the fresh condition, may be precipitated by alcohol or acetic acid. At certain points there are masses of small green bodies, which will afterwards be recognised as blood corpuscles (small hæmorrhages).

Under the high power (× 300) observe the fibro-cellular trabeculæ, which, at their margins, gradually merge into the myxomatous structure. Examine the branching cells more closely, and note the granularity of the protoplasm, the number and ramification of the processes, and the intercellular spaces, in which now may be observed a number of small round cells. Examine the blood corpuscles, which have escaped from the blood-vessels and are in various stages of disintegration. In the breast, the myxomatous tissue may spread between the acini of the gland, whilst in some specimens it is found

to encroach on the acini, growing into them and distending them, as does granulation tissue in certain cases, when it forms the so-called cystic sarcoma.

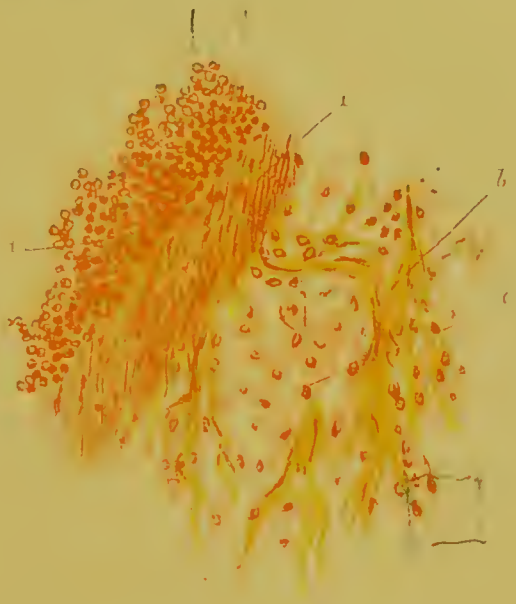


FIG. 101.—Drawing of myxoma of breast. Section stained with picro-carmine. (× 250.)

a. Thick fibrous band bounding space on one side.
b. Thinner fibrous trabecula bounding space on other side.
c. Branching nucleated myxomatous cells, with spaces (filled with mucin) between them.
d. Sarcomatous looking tissue near the thick fibrous band.

Forms of myxoma:—(1.) Pure myxoma: (*a.*) Hyaline form, exceedingly translucent substance, with few round cells between the branching cells; (*b.*) Medullary form, which is more opaque from the presence of a greater number of the small round cells.

(2.) Myxoma containing a quantity of elastic tissue.

(3.) Lipomatous myxoma, in which some of the branching cells are distended with droplets of oil.

(4.) Cystic myxoma, from softening of certain portions of the tumour.

Degenerations.

(1.) Hæmorrhagic—(see above, p. 382).

(2.) Mucous and colloid degeneration of the cells.

(3.) Inflammation which may become gangrenous, and ulceration, especially where the tumour is polypoid, and therefore on a free surface and exposed to mechanical injury.

Glioma.

249. Two forms of glioma are usually described, but as one of them appears to be in fact a form of small round-celled sarcoma, its consideration may be deferred. The true glioma, as met with in the brain and spinal cord, is seen as a gelatinous looking mass, which is evidently of slow growth, gradually replacing the nerve tissue, into which it merges at its margins. It varies from a grey translucent mass to greyish or dark red, according to its vascularity. It may be distinguished from the small round-celled sarcomata, which frequently occur in these positions, by the fact that even in the form where hæmorrhages occur (the dark vascular form) the substance is usually very firm. They are non-malignant, and occur more frequently in the brain than in the spinal cord, and in children than adults.

Harden in Müller's fluid and spirit (§ 54, p. 43), cut sections (§ 67, p. 48), stain in carmine (§ 75, p. 58), half clear up (§ 238, p. 364), and mount in dammar varnish. This method of half clearing up, as in the cord, brings out the processes of the Deiter's or neuroglia cells very distinctly.

Examine under a low power (× 50), and note that the tumour is composed of a mass of neuroglia cells, the nuclei of which are very distinctly seen. Between them is a tissue the structure of which cannot be determined under this power. Running through the mass are small blood-vessels, around which the deeply stained nuclei are grouped.

Under the high power (× 300), examine a few of the cells teased out after staining with picro-carmine. They are found to be composed of granular looking protoplasm, imbedded in which are one or two rounded or ovoid nuclei. From the main body of the cell branching processes run out, which are very like those met with in the myxoma. Examine the hardened and half cleared up section. Observe the capillary blood-vessel with its endothelial plates, and the branching cells with their large nuclei, and their long, delicate, and anastomosing process. If a section be stained and mounted by any of the ordinary methods, the nuclei can be seen quite readily, but the tissue between appears to be composed of a felted mass of fibrils seen in

longitudinal sections, or as a granular mass, where the transverse sections of the fibrils are numerous. As already seen in the epileptic

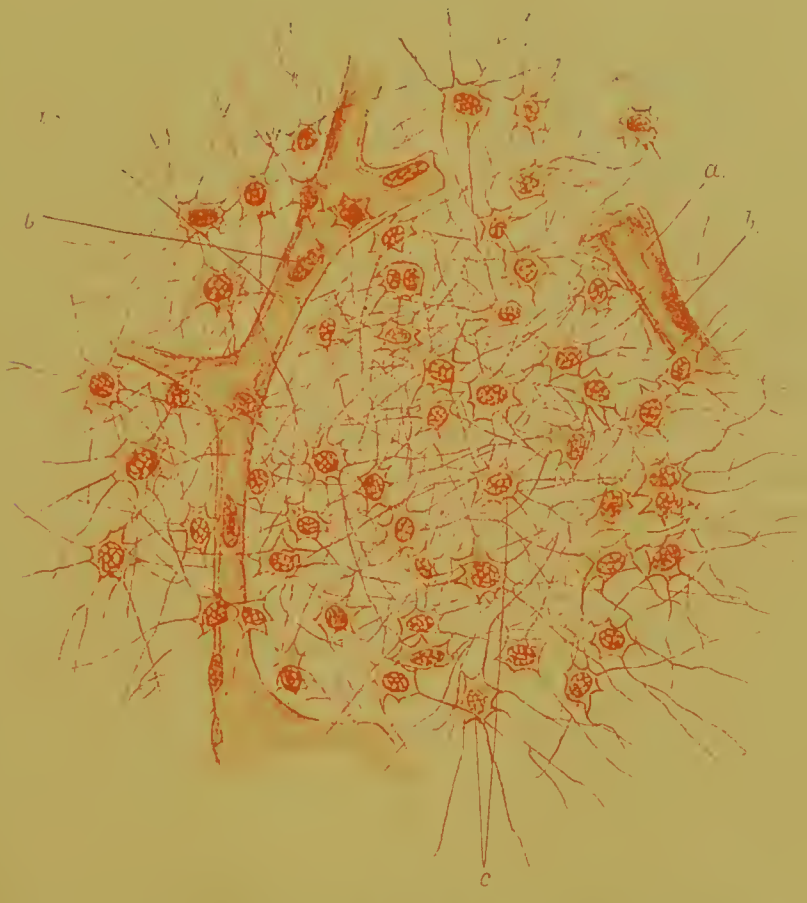


FIG. 102.—Glioma taken from the brain. Section stained with carmine, and half cleared up. (× 600.)

a. Capillary blood-vessels.
b. Nuclei, with intranuclear plexus well seen.
c. Neuroglia cells, or Deiter's cells, with nuclei (in which the network is well seen) and long branching processes.

medulla, this gliomatous tissue may be greatly increased in that condition, and a similar tissue is found in large quantities in the dense walls of old cysts in the brain. It is a connective tissue tumour, composed of neuroglia. The vessels in this growth are frequently dilated at various points, or the dilatation may be general.—(Ziegler.)

Degenerations.—Hæmorrhagic (as in myxoma), fatty, caseous, or simple softening may occur.

Lipoma, or Fatty Tumour.

250. Fatty tumours grow most frequently in connection with pre-existing fat, and are therefore most frequently met with in the subcutaneous tissue, especially in such parts as are subjected to pressure, as on the shoulders or buttocks. They are also found in the subcutaneous tissue of the abdomen, in the breast, and as the aborescent lipomas of the synovial fringes of joints. They are sometimes found, nevertheless, in tissues which do not normally contain fat, as in the dura mater, and in the submucous tissue of the intestine, and cases are recorded of fatty tumour of the liver and heart, and of its occurrence between muscles, in bone, and other places where it would not be expected. The lipoma is of slow growth, and may be solitary or multiple. It is usually seen as a rounded and lobulated or flattened mass, from the size of a hazel nut, or smaller, up to a growth of many pounds weight, surrounded by a well-formed fibrous capsule, from which septa run in and cut the fatty mass into a series of lobules, and to the naked eye it presents the appearance of a mass of yellow fatty tissue, through which run the white and glistening fibrous septa containing the blood-vessels which supply the growth. The fatty tissue of a lipoma is much softer and more plastic than ordinary fatty tissue. It may also occur in a pedunculated form, as in the fatty synovial fringes, and in enlarged appendices epiploicæ.

Harden in chromic acid (§ 57, p. 44), or Müller's fluid and spirit (§ 54, p. 43), stain sections in picro-carmine (§ 73, p. 53), and mount in Farrant's solution (§ 98, p. 71).

Under the low power (× 50) note that the tissue very closely resembles ordinary adipose tissue, but that at certain points there are, in addition to the connective tissue cells distended with fat, numerous embryonic cells, in which the process of fatty infiltration is as yet incomplete. Here and there are groups of these small, deeply stained cells in which there is not a single droplet of fat. Note how free the vascularity of the tissue is, and also that the fat cells are rather larger than in the normal adipose tissue.

Under the high power (× 300), the swollen or infiltrated connective tissue cell is seen with its nucleus pushed in to an angle, and the protoplasm of the cell forms a thin film or coat around the

globule of fat. The fat cells in some cases contain fat crystals, and in many instances they are so closely packed together that they

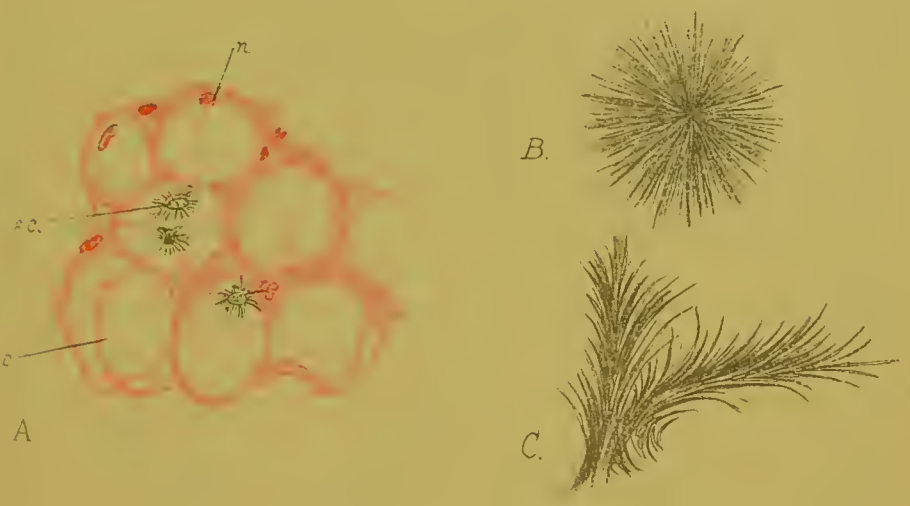


FIG. 103.—*A*. Lipoma. (× 200, after Cornil and Ranvier. Am. Ed.)
n. Nucleus of fat cell.
p. Thin film of protoplasm surrounding fat globule.
f.c. Crystallised fatty acids (margarin).
B. Free tuft of margarin needles. (× 300, after Ziegler.)
C. Feathery needles of "margaric acid," or margarin. (× 300, after Ziegler.)

assume a polygonal form. Under this power a number of the uninfiltrated cells are seen to be myxomatous in type.

Varieties of lipoma.—(1.) Pure lipoma—the form described.

(2.) Myxomatous lipoma, in which the myxomatous cells are numerous.

(3.) Fibrous lipoma, in which the fibrous trabeculæ are very large and very numerous.

(4.) One case of osseous lipoma is described by Cornil and Ranvier, in which were osseous trabeculæ.

(5.) Erectile lipomas—very vascular fatty tumours, principally met with as polypoid growths on serous and mucous surfaces.

Degenerative changes in lipoma.—(1.) Molecular softening may occur when the tumour becomes opaque and putty-like. (2.) Calcareous degeneration. (3.) Inflammation and ulceration, where young connective tissue cells are formed more rapidly than they are infiltrated.

Fibroma.

251. Of the two forms of fibroma—fasciculated and lamellar—the fasciculated is perhaps the more characteristic. It occurs most frequently as a firm, dry, glistening, white or brownish, not very vascular tumour. It may be rounded or lobulated, has a capsule, and on section presents a peculiar appearance, often compared to watered silk. In other cases the tumour is not so firm, is somewhat more pink, and is more gelatinous looking. When a cut surface of the drier form is scraped, very little fluid is removed by the knife, but small fragments of the tumour are removed, which may be examined fresh, and are then seen to be composed of small bundles of connective tissue. Treat one of these fragments with acetic acid, and watch it under the high power of the microscope; the connective tissue bundles are seen to swell up, become gelatinous or homogeneous, and leave the connective tissue cells to be seen as branching nucleated masses of protoplasm.

Make a more careful naked eye examination before putting the tumour to harden, and notice that there is a lobular arrangement; that each lobule is composed of a number of concentric layers of fibrous tissue; that the lobules are softer towards their centre, at which point they seem to grow; and that between the lobules is a quantity of ordinary connective tissue, in which run numerous blood-vessels.

Harden a piece of the tumour in Müller's fluid (§ 53, p. 42), or in methylated spirit (§ 52, p. 42), cut sections (§ 67, p. 48), stain in picro-carmine (§ 73, p. 53), and mount in Farrant's solution (§ 98, p. 71).

Examine under a low power (× 50), and note that the tissue is throughout stained a beautiful pink (a colour very characteristic of fibrous tissue). The fibrous tissue has different arrangements in different parts of the tumour; but the greater part of it is disposed in bundles, which run in various directions, or in bundles which are arranged concentrically, or the fibres have a peculiar feather-like or ladder-like arrangement. In the last-named form there are bands of dense pink fibrous tissue, which may be said to run longitudinally; whilst running off at more or less acute angles are more delicate bands of pink tissue.

In the dense longitudinal bands there are few cells; but between the transverse bands numerous nuclei of cells may readily be observed under this power. Whatever be the arrangement of the fibres, the cells—small, round, elongated, or branching—are always most numerous in the more open tissue. There are never any yellow elastic fibres present. Observe that the blood-vessels are not very numerous, but that they are all well formed. In a molluscum fibrosum, where there is a kind of œdema of the fibrous tissue, the arrangement of the fibres and the cells can be very easily discerned.

Examine under a high power (× 300) for the pink fibrous bundles, between which are branched cells, the processes of which clasp the



FIG. 104.—Granulation cells, becoming developed into fibrous tissue. (× 500, after Ziegler.)

a. White blood corpuscles, with a single nucleus.
*a*¹. With several.
b. Formative cells of various shapes.
c. Formative or connective tissue cells, with two nuclei.
*c*¹. With numerous nuclei (giant cells).
d. Formative cells, with developing fibrillar periplast.
e. Developed connective or fibrous tissue.

bundles of fibrils. Observe how scanty are the cells in the dense pink fibrous part, and how numerous they are in the soft growing parts of the tumour. Examine the cells; some are merely round embryonic cells, all nucleus; others are surrounded by a quantity of protoplasm;

others are elongated, and the formed material around them is becoming fibrillated; others again have several nuclei; and some have well developed branching processes. In fact a young or growing fibroma is one of the best structures in which to study the development of fibrous tissue, as it is composed of the purest form of that tissue. The cells under examination, as was seen under the low power, are always most numerous in those parts of the tumour where the fibrous tissue is most open. Consequently they are found in greatest profusion between the transverse bars of the ladder.

Fibrous tumours are of comparatively slow growth; they are non-malignant, and, as a rule, grow where fibrous tissue already exists. Their most frequent positions are the subcutaneous and submucous tissues; in the upper and posterior part of the pharynx (then probably growing from the periosteum of the basilar process); in fasciæ, and in the interfascicular tissue of nerves; in the ovary; in the uterus; as small, firm, rounded masses, about the size of a pin's head, or larger, in the centre of a pyramid of the kidney; as keloid growths in scars; and as the so-called loose cartilages of the knee joint.

The changes to which they are liable are—serous infiltration, as in the molluscum fibrosum; mucoid degeneration of the fibres; fatty degeneration, especially in fibromas of syphilitic origin (Cornil and Ranvier); and calcification. The two changes last named occur near the centre of the nodules, or away from the blood-vessels. Inflammatory changes and new cell formation are sometimes induced, especially when the tumour from its position is exposed to mechanical injury.

The Lamellar Fibroma or Flat Fibroma.

252. Flat fibromas can scarcely be looked upon as true fibromas. They are rather a thickening of lamellar tissue—the result of a chronic inflammatory process on a serous surface. They are met with as flattened hard cartilaginoid masses, which vary considerably in size and shape. They occur on the outer surface of the spleen and liver (especially after abdominal dropsy); on the pleura, or in the subpleural tissue; in old people; in stone-masons' lung; and on the inner surface of blood-vessels in certain conditions. They are

usually yellow and translucent, but they may be pigmented; they are cartilaginous in consistence, and are cut with difficulty.

Harden in Müller's fluid (§ 53, p. 42), cut at right angles to the shortest diameter of the growth (§ 67, p. 48), stain the sections with picro-carmine (§ 73, p. 53), and mount in Farrant's solution (§ 98, p. 71).

Examine under a low power (× 50). The structure is essentially that of corneal tissue, or the inner lining of vessels. It consists of a series of lamina of fibrillated tissue, between which are flattened cells. Under a high power (× 300) these flat cells are perceived to be only flattened branching connective tissue cells, seen in profile.

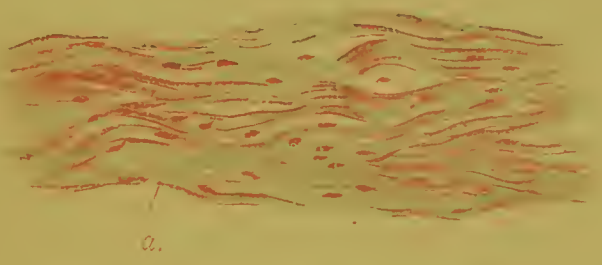


FIG. 105.—Lamellar fibroma, stained with magenta. (× 100.)
a. Fibrous lamellæ.
b. Nuclei of connective tissue cells lying between the lamellæ.

That these cells may be observed, a small fragment must be treated with acetic acid, and then carefully teased out, and stained with carmine (§ 75, p. 58).

CHONDROMA.

253. Cartilaginous tumours are usually met with as multiple growths, either rounded or lobulated, surrounded by a fibrous capsule, with fibrous bands, separating the lobules from one another. They usually grow from the periosteum of bones (especially ends of the metacarpal bones, on the phalanges of the fingers and toes); in the bones themselves; in the parotid and other salivary glands; in the testicle, skin, lung, or mamma. They are usually firm and elastic, though in some cases, owing to mucoid degeneration, they are soft, and even gelatinous. On section the tumours cut with the peculiar creak of cartilage; or if there is calcification, there is also a gritty feeling.

Running across the section are seen white glistening fibrous bands, whilst between these the cartilage proper has a translucent, pearly appearance, with a bluish or pink tinge.

Take a piece of tissue from a chondroma of the parotid gland, in which there is considerable calcification towards the centre of the lobules; harden in methylated spirit (§ 52, p. 42), stain in picro-carmine (§ 73, p. 33), and mount in Farrant's solution.

Examine under the low power (× 50). The capsule is a pink fibrous mass at the periphery, at one margin of the section. From this capsule a series of fibrous trabeculæ, in which run small vessels, extend between the masses of cartilage. Even under this power the character of the cartilage cells may be seen. Some appear to be rapidly developing hyaline cartilage cells, with well-formed cartilage capsules; whilst in other cases the capsules have disappeared, and branching cells are sending their processes in all directions into the matrix, which here appears to be softer and mucoid; it takes on the staining very delicately indeed. Near the centre of each lobule calcification is commencing, and the tissue appears to be green, and much less translucent. At the margin of the calcified part the granules of calcareous material may be seen imbedded in the matrix, whilst in some few cases the calcareous particles appear to have found their way into the capsules.

Under the high power (× 300), the hyaline cartilage, with its encapsuled and proliferating cells, must be looked for, the matrix of which in this case is not fibrillated. The branching cells in the mucoid matrix, and the fibrous capsule and trabeculæ, with the well developed blood-vessels, are also to be looked for. The green part with the highly refractile calcareous particles infiltrating the matrix around the distended capsules can also be well seen under this power.

In another section of a parotid tumour growing more rapidly and of softer consistence, hardened and treated as directed, the tissue may be seen to be composed almost entirely of branching cells imbedded in a mucoid matrix, with proliferating gland structure running through it. The epithelium of the gland acini and ducts takes part in the increased activity of the surrounding tissues, and grows so rapidly that it forms solid-looking columns or masses, which intersect the

myxochondromatous tissue in all directions. This form of parotid tumour is spoken of as the myxochondro-adenoma.

Myxochondroma.

254. In certain cases cartilaginous tumours, much softer and more gelatinous than the form last described, growing with extreme rapidity, and frequently giving rise to similar growths in other parts, occur. This—which in many respects resembles a sarcoma more than a chondroma—has been sufficiently fully described. In the case from which the section now described was taken, the tumour grew from the periosteum of the scapula, increased very rapidly in size, and gave rise to secondary growths of a similar nature in the lung, in the branches of the pulmonary artery. It was a soft lobulated tumour, composed of a brown gelatinous material surrounded by a very vascular fibrous capsule. Hardening and mounting as before, and examining under a low power, the pink fibrous capsule and trabeculæ are readily seen, and running in them are well-formed blood-vessels. Near the trabeculæ the cells are somewhat flattened, and have a rather regular arrangement. Towards the centre of the mass are large cells, very irregular in shape, having long processes, and often two, three, or four nuclei and nucleoli. Between these huge cells, which by Ranvier are compared to the cells of the cartilage found in cephalopods, the matrix is somewhat fibrillated near the periphery, but mucoid towards the centre. Towards the periphery greenish masses (coloured blood corpuscles) may be seen.

Examine under the high power (× 300) for detail.

Other varieties of cartilage, such as white fibro-cartilage, may be met with in these tumours, and all intermediate forms between that and the hyaline are found.

Degenerations.—(1.) Mucoid softening of the matrix; (2.) Calcification of the matrix; (3.) True bone formation.

Osteoma.

255. Osteomas are outgrowths of bone, chiefly at the point of junction between the bone and its cartilage. They are classified according

to their position into exostoses, or those growing from the exterior of a bone, and enostoses, or those growing in the interior. A more natural classification is that which arranges them according to their structure.

The first form, or the *eburnated osteoma*, appears to be a syphilitic growth from the inner table of the skull. These are extremely hard, are often multiple and symmetrical. Prepare in v. Ebner's solution (§ 65, p. 46), cut sections, and stain in picro-carmine. Notice that the dense bony structure is composed of lamellæ parallel to the surface of the tumour.—(Virchow.) In these lamellæ there are no blood-vessels and no Haversian canal; but, according to Cornil and Ranvier, there are canaliculi similar to those found in the cement of teeth, which run towards the surface.

The compact osteoma is composed of ordinary compact bone, similar to that found in a long bone. It is met with as a nodular growth, usually beneath the periosteum, or in the periosteum of long bones; but it may be found growing in the substance of the bone, in the meninges of the brain, in the choroid, in the pericardium, in the skin around glands, in the apices of tuberculous lungs, even in the nerve centres; but such tumours may be met with in tendons, in intermuscular septa, and in other positions where there are new fibrous tissue formations. When the growth is cut with a saw, and examined with a low power lens, the vessels and Haversian canals will be found to run at right angles to the long axis of the bone.

Prepare in chromic and nitric acid fluid (sub-sections § 63, p. 46), or in picric acid (§ 61, p. 45). Stain in picro-carmine (§ 73, p. 53), and mount in Farrant's solution.

Notice that the structure is essentially that of compact bone, that the vessels run in Haversian canals at right angles to the long axis of the bone, that there is a periosteal fibrous covering, with a layer of cells and young bone formation beneath. Around the Haversian canals the regular Haversian systems may all be readily distinguished in this specimen.

The spongy osteoma differs from the compact form only in the fact that the trabeculæ are much thinner and not so numerous; that the medulla is usually more embryonic in character, and appears to the naked eye as a gelatinous mass. In some cases, however, it is fibrous.

Under the microscope some adipose cells can usually be observed amongst the small round cells which compose the embryonic mass. It is in fact very like the spongy tissue of which the ends of long bones and the shorter ones are composed. Treat as for compact osteoma, and examine.

MYOMA.

256. The muscular tumour is usually described as of two forms.

1. That composed of striped muscular fibre, which is an exceedingly rare condition, and is probably met with only as a result of the higher development of sarcomatous tissue, in which case the muscle is imperfectly developed, and never gets beyond an embryonic type.

2. The true myoma or leio-myoma, in which there is a formation of well developed non-striped muscular fibres. These tumours are met with so much more frequently in the uterus than in any other position that they have been named uterine fibroids. They may, however, occur in any position in which non-striped muscle is normally present, as in the gastro-intestinal tract, where they are seen as polypoid growths; in the wall of the bladder; in the prostate in old men; in the skin, especially of the scrotum; and in the kidney, where they commence near the apices of the papillæ. These tumours may be small, when they are rounded, or they may grow to a considerable size, when they become lobulated. Like most of the simple and slowly growing tumours, they are enclosed in fibrous capsules. They are usually multiple, and may grow to an enormous size.

The typical uterine fibroid is a firm, fleshy, somewhat elastic mass growing in the muscular wall of the organ, in which case the tumour is usually paler, but sometimes brighter in colour than the surrounding muscular tissue. In the smaller rounded tumours the muscular tissue is arranged in concentric laminæ, an arrangement which can be easily discerned with the naked eye; but in the larger lobulated forms each lobule is composed of one of these concentric masses, and between them are the bands of fibrous tissue which run from the capsule, and in which may be seen the blood-vessels which pass into and nourish the new growth. In consequence of this laminated arrangement, the masses are frequently compared to balls of cotton in appearance. In the uterine wall the tumours occur in three

positions :—(1.) Growing in the muscular wall itself—the intramural form; (2.) Growing from the muscular tissue, beneath the mucous membrane (this, the submucous myoma, grows into the uterine cavity as a pedunculated mass, which pushes the mucous membrane before it); and (3.) A similar polypoid growth on the outer surface of the uterus, which pushes before it the peritoneal membrane, subserous or subperitoneal myoma.

Harden a piece of this tumour in Müller's fluid (§ 53, p. 42), cut sections (§ 67, p. 48), and stain in picro-carmine (§ 73, p. 53), or eosine and logwood (§ 79, p. 62), and mount in Farrant's solution (§ 98, p. 71), or in Canada balsam (§ 96, p. 69).

Examine under a low power (× 50). In pure myoma the section, instead of presenting a pink appearance, as in the fibroma (with picro-carmine), has a yellowish brown colour, with minute crimson points at intervals. In an old myoma, where there is usually a considerable quantity of fibrous tissue, the pink strands stand out prominently between the yellowish brown bands. In any case, the



FIG. 106.—Non-striped myoma (uterine fibroid). Stained with picro-carmine. (×450.)

a. Mass of non-striped muscular tissue, in which the rod-shaped nuclei and the parallel arrangement of the fibrils are seen.
b. Similar bundles of fibres cut transversely. The sections of the fibrils have the appearance of rounded cells, the section of the round nucleus is seen as a dot in *some* of the sections.
c. Spindle-shaped cells, of which the fibrils (*f*.) are composed.
d. Pink fibrous tissue.
e. Connective tissue corpuscles.

muscular fibres are so small that it is necessary to use a somewhat higher power than usual to bring out the detail of the structure.

(× 450.)—Notice that the muscular fibres are identical in appearance with those of ordinary non-striped muscular tissue, but that the bundles of fibres interlace with one another in every direction. Each bundle is marked by a series of parallel lines, and if the tissue is dissociated, or if the edge of a section be examined, each fibril marked off by the parallel lines may be seen to be composed of spindle-shaped cells, which overlap at their ends to form the fibres. A rod-shaped nucleus may be seen in the centre of each cell. The bundles of muscular fibre are usually thrown into folds, so that though the lines are parallel they are somewhat wavy. In certain parts of the section the fibres are cut transversely or obliquely, and in place of parallel lines there are bundles of what appear to be rounded cells, some with a deeply stained centre, others without. They are simply the muscle cells cut transversely, the section sometimes passing through the rod-shaped nucleus, and sometimes not. To distinguish between a true fibroma and a fibro-myoma is not always an easy matter. It is therefore well to bear in mind that the fibrous tissue is white, hard, and glistening, whilst the muscular bands may be "pink, reddish grey, or white," and are not nearly so firm. To make certain, small fragments of the tissue should be treated with a twenty per cent. solution of nitric acid for twenty-four hours, or for half an hour in a thirty or forty per cent. solution of caustic potash. The fibrous tissue then swells up and disappears, and the muscular fibres may be separated and examined, stained or unstained. The rod-shaped nuclei stand out very prominently in such preparations.

Degenerative changes.—Hæmorrhages are very common, owing to fatty or mucoid softening, especially where the vessels are numerous. Calcification frequently takes place, giving rise to the so-called womb-stone. Inflammation in consequence of injury also occurs, and abscess formation, in which condition the fibres undergo cloudy swelling, becoming swollen and granular.

Neuroma.

257. It is necessary to mention this tumour, although it is of comparatively rare occurrence. It may assume one of two forms—(*a*) composed of nerve fibrils occurring at the cut ends of nerves;

or (*b*) composed of ganglion cells, one case of which is recorded in connection with the supra-renal capsules. Many of the so-called neuromas are in reality fibromas or myxomas on the nerve trunks, or gliomas in the central nervous system.

Prepare as for nerve structures (§ 241, p. 372).

Angioma.

258. The angioma is a tumour made up of dilated blood-vessels, some of which appear to be of new formation, whilst others are only pre-existing blood-vessels dilated. Along with the dilatation there is frequently an increase in the amount of connective tissue.

There are two forms of angioma—the cavernous and the simple. The cavernous form has been already described under the heading of Liver (§ 129, p. 126), and the structure of cavernous angioma of the skin (kidney, spleen, uterus, muscles, bones, and hollow viscera—rarer positions) is very similar, making allowance for the difference in the structure of the organ in which it occurs. Prepare as recommended in § 129.

Simple angioma is distinguished by the fact that although there are fusiform and sacculated dilatations of the new or pre-existing vessels, the general tubular form of the vessel is not lost. In the simple angioma or nævus of the skin (mother's mark) the dilatation above described is the principal feature, as there is little thickening of the walls of the vessels. Seen with the naked eye, such a tumour appears as a bright red or livid patch surrounded by a number of small similar spots. These patches are not raised from the skin, in which they most frequently occur. Only very rarely are such tumours met with in other positions, as in the mamma, bone, and the brain. In gliomata they are comparatively common.

In another form of simple angioma the dilatation is not so great, but the increase of tissue around the vessels is more marked, whilst hæmorrhoids, composed of masses of small dilated veins, with thickened walls, are formed in the submucous tissue of the rectum, and supported by an increased quantity of connective tissue. Harden and prepare as for nerve structures. On microscopic examination the principal points to note are in all cases the dilated saccules, con-

nected by the vascular tubes; the well-marked endothelial lining of the blood-distended cavities; and in some cases the thickening of the vascular walls, chiefly by an increase in the thickness of the adventitia.

A similar condition of the lymphatic vessels is described under the term Lymphatic Angioma, or Lymphangioma.

Lymphoma.

259. The true lymphoma cannot be omitted from the consideration of the histioid tumours, and along with this must be taken up two other forms of lymphoid growth, both of which depart somewhat from the true histioid type, and, unlike the true lymphoma, are often very malignant—the lymphadenoma and lympho-sarcoma.

The lymphoma frequently appears to be rather a hyperplasia of lymphoid tissue than a true tumour, and it is always found in positions in which lymphoid tissue is normally present, as in lymphatic glands in the intestine, in the uterus, kidney, &c.; but occasionally there are true tumour growths, composed of adenoid tissue. It usually occurs as a solitary mass, which does not attain any great size, and is situated in one of the positions previously mentioned. It is usually surrounded by a more or less dense fibrous capsule. On section it is uniformly soft, and white or pinkish white in colour. Where small hæmorrhages have occurred, it may have yellow or brownish points (altered blood pigment). From this fact, along with the general appearance, it may in some cases be mistaken for a sarcomatous growth; but the history and histological structure will at once set any doubts at rest.

Harden a piece of the tumour in Müller's fluid (§ 53, p. 42), or in methylated spirit (§ 52, p. 42), stain in picro-carmine (§ 73, p. 53), and mount in Farrant's solution (§ 98, p. 71).

Examine under the low power (× 50), and note that the tissue is essentially like normal adenoid tissue. The deeply stained nuclei of the lymphoid cells are seen in great numbers; here and there running through the mass may be seen capillary vessels. If one of these vessels be examined near the edge of the section, delicate bands of pink tissue may be seen attached to its walls; and in favourable specimens, where the rounded cells have been displaced, a deli-

cate reticulum may be seen. At the junctions of the strands of the network the nuclei of cells are situated, evidently lying on the strands or fibrillæ. A number of larger vessels are also present, with the fibrils attached to their walls. To distinguish more clearly the elements of which the tissue is composed, it is necessary to shake a thin section of the tumour in a test tube containing a small quantity of three-quarter per cent. salt solution (§ 34, p. 32), lay out carefully on a slide, stain with eosine and logwood (§ 79, p. 62), and mount in glycerine (§ 97, p. 70), or in Canada balsam (§ 100, p. 72). The stroma attached to the capillary walls can then be readily distinguished. It is said that in the lymphoma the capillaries are distended, but this is extremely difficult to determine.

Examine both sections under the high power (× 300). The attachment of the stroma to the capillary walls is more easily seen. At the junctions of the bands of the stroma there are large branching endothelioid cells, each of which has one or two distinct nuclei. The processes of the cells clasp the bands of stroma, and the cells are placed on the fibres, and although their processes may extend on them for some distance, they are quite distinct from the fibres (Fig. 39). Ranvier holds that these endothelioid cells are the cells by which the fibrillæ are secreted or formed. This is an important fact, to be borne in mind when the consideration of the other forms of lymphoid tumours is approached. Under this power the deeply stained nuclei stand out very prominently. Lying in the centre of the network are the small round lymphoid cells, which are stained almost throughout, which shows that they are composed chiefly of a nucleus. The zone of protoplasm around this is extremely thin. In this respect, then, they differ from leucocytes. Some of the cells are larger, and may contain a couple of nuclei, and in a few instances, especially where there have been small hæmorrhages, they may contain granules of pigment. Where the capillaries have given way, the blood may be seen as greenish corpuscles, with their double outlines, lying in the meshes around the ruptured capillary.

Lympho-Sarcoma.

260. The second form of lymphoma—the lympho-sarcoma—is a malignant growth, which, from its clinical history and pathological

appearances, is frequently mistaken for a sarcomatous or soft cancerous tumour. The tumours may grow in any position, but commence usually in the lymphatic glands or tissue of the viscera, and then spread, especially to the lungs. The so-called primary cancer of the kidney is nothing more than a lympho-sarcoma. They are multiple, and may grow to a considerable size. The section from which the description was taken was removed from one of the mesenteric glands.

To the naked eye the growth very much resembles an ordinary lymphoma; but it is more pink, slightly more vascular, and of a rather softer consistence throughout. Around the somewhat diffluent mass is a delicate fibrous capsule. Over the surface of the section are numerous yellow or brown spots, very similar to those which have already been described, and to those which will be described as present in the softer forms of sarcoma. These are due to rupture of the vessels and extravasations of blood at different periods. Scrape the surface with a knife, when a quantity of creamy fluid will be removed. Examine this in a neutral solution (§ 34, p. 32) under a high power, and note that it is composed chiefly of lymphoid cells, similar to those described as occurring in lymphoma.

For microscopic examination shake a thin fresh section in a test tube with some of the neutral solution, spread the section out on a slide, stain with picro-carmine (§ 73, p. 53), and mount in Farrant's solution (§ 98, p. 71). Also examine a section hardened in Müller's fluid (§ 53, p. 42), stained and mounted as above.

In the hardened section the lymphoid cells predominate to such an extent that no other structure, except a few blood-vessels, can be distinguished, either under the low or the high power. Around the blood-vessels the green hæmorrhagic masses may be seen. Under this examination the tumour still resembles the small round-celled sarcoma (§ 268, p. 414).

Now examine the pencilled or shaken specimen. Under the low power (× 50) a few of the small blood-vessels may be seen, and at certain points, where the lymphoid cells are washed away, an exceedingly delicate reticulum can be distinguished. This reticulum is similar to that which is present in lymphoma, but is much more delicate; the meshes are larger, and the endothelioid plates are neither so prominent nor so numerous. In the small round or ovoid cells the

nuclei appear to be undergoing more rapid division, and therefore much more frequent multiplication, though this can scarcely be recognised without the aid of the high power (× 300). Under this power the increased proportion of small round cells to reticulum can be appreciated, and also the relatively small number of endothelioid plates on the network. Also note the small masses of coloured blood corpuscles, the result of hæmorrhage from the delicate and badly supported vessels.

Lymphadenoma.

261. In Hodgkin's disease, as already seen (Liver, § 124, p. 119; Spleen, § 216, p. 322), there is an overgrowth of certain elements of the lymphoid tissue. This disease commences as a primary tumour growth in the lymphatic glands, generally of the neck or groin. From the primary centre, first the surrounding glands and then the various viscera are involved in a malignant infective process, by which secondary tumours are formed. In this way the spleen, liver, kidneys, lung, submucous tissue of the intestine, serous membranes, skin, heart, and supra-renal capsules, are all in turn affected. In the lymphatic glands the lymphadenomatous tissue is firmer and not so liable to caseate as when it occurs in the viscera, but otherwise the growths are identical in both their naked eye and microscopic appearance. The tumours vary considerably in size. They often occur as small masses, but they may be present as large pinkish white nodules, though in the liver, spleen, and kidneys, especially where there is a tendency to caseation, there is a yellower tinge from the commencement. These nodules are firm and elastic at first, but where caseation is setting in they become doughy, and even putty-like. Hæmorrhages into this growth are comparatively rare.

From the description of lymphadenoma of the spleen (§ 216, p. 322), a fair idea of the microscopic appearances may be gathered. It will be remembered that in that organ there was an enormous increase in the amount of the fibrous stroma or network, with a corresponding increase in the number of endothelioid plates, which in this condition appear to be particularly active, whilst the number of lymphoid cells is comparatively small. The cells appear to be compressed out of existence by the enormously increased fibrous tissue.

Examine a section of lymphadenoma taken from any of the lymphatic glands, hardened in Müller's fluid (§ 53, p. 42), stained in picro-carmine (§ 73, p. 53), and mounted in Farrant's solution (§ 98, p. 71), when much the same appearances will be seen under both high and low powers. In the growing part of the tumour occurs a great increase in the number and activity of the endothelioid cells, followed by an increased thickness and number of the bands of the reticulum, which is gradually converted into a mass of fibrous tissue, and the lymphoid cells become more and more sparse as the fibrous tissue is more fully formed. As in the spleen, the lymphadenomatous tissue gradually invades and destroys the surrounding tissue.

It may be of some assistance to the student if a short *resumé* of the principal points of difference (from a structural point of view) of these tumours be given.

Lymphoma—ordinary lymphoid tissue; reticulum well developed; endothelioid plates also well developed; number of lymphoid cells normal.

Lympho-sarcoma—scanty reticulum; corresponding diminution in the number of endothelioid plates; enormous increase in the number of lymphoid cells.

Lymphadenoma—reticulum in excess, and becoming fibrous; early increase of reticulum, accompanying increased number and activity of the endothelioid plates; when tissue is becoming fibrous, great diminution in number of lymphoid cells.

From the above statement it will be seen that, as in connective tissue, the quantity of the reticulum varies directly as the number of endothelioid plates, but that the same rule does not hold good in regard to the lymphoid corpuscles.

Simple Histioid Tumours composed of more than one Tissue.

Papilloma.

262. The papilloma—under which heading are classed warts, horns, the compound cauliflower excrescences, and such polypoid growths as occur in the bladder and in the larynx—consists essentially of a hypertrophied and often branched papilla, covered by a hypertrophied layer of epithelium. The ordinary wart will be readily recognised, as will also the large cauliflower-like excrescences which are so fre-

quently met with round the anal or genito-urinary orifices in syphilitic and gonorrhœal patients. Although this tumour may grow rapidly, it is non-malignant, and is of purely local origin. Horns are usually seen on the face and neck, and are in most cases multiple. Take small pieces of one of the compound cauliflower excrescences and harden in Müller's fluid (§ 53, p. 42) for the examination of the vessels; a second in picric acid (§ 61, p. 45); and a third in methylated spirit (§ 52, p. 42)—the two latter for the examination of the epithelium; cut sections (§ 67, p. 48), stain in picro-carmine (§ 73, p. 53), and mount in Farrant's solution (§ 98, p. 71).

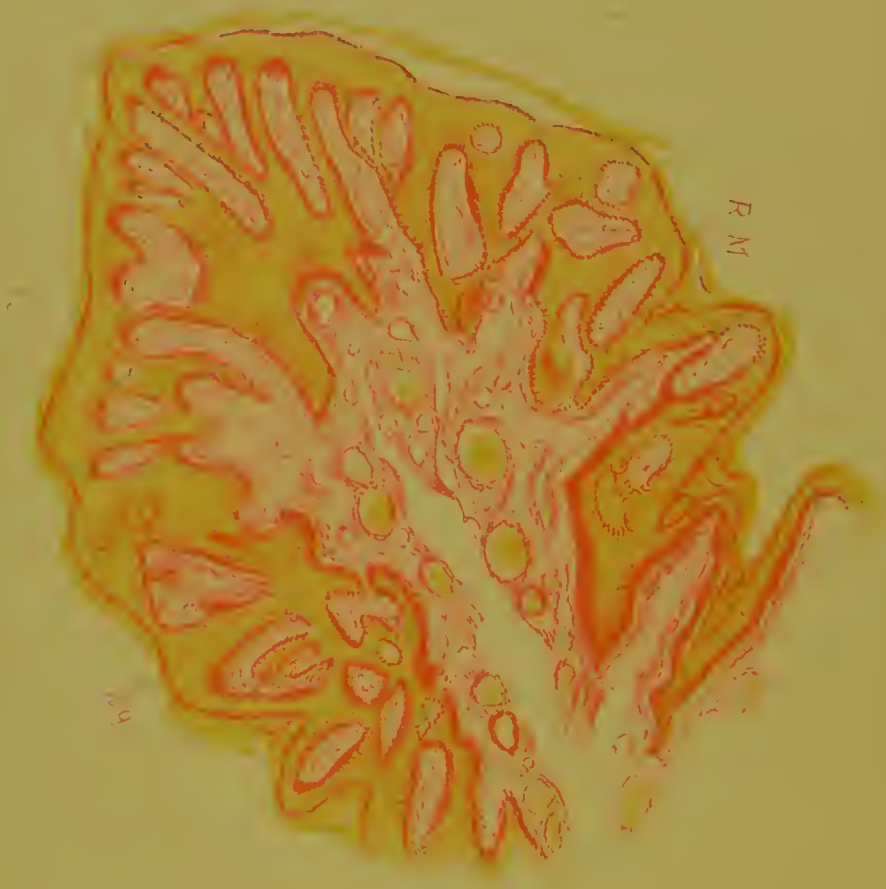


FIG. 107.—Section of papilloma. Stained with picro-carmine. (× 50.)

c. Horny layer.
R.M. Rete Malpighii.
C.t. Connective tissue basis.
b.v. Blood-vessels of considerable size.

Examine under a low power (× 50). The general outline of the growth must first be noticed. In place of the simple papilla there is a

branching and rebranching mass of tissue. The basis is fibrous or fibro-cellular tissue. This, in the picro-carmine stained specimen, is pink, if fibrous, but more crimson if the cells predominate, as where the tumour is of very rapid growth. Supported in the fibrous basis are numerous blood-vessels, very similar to those met with in a normal papilla, except that they are usually somewhat larger. At the point of junction with the subjacent tissues these vessels appear to open into large vascular sinuses or dilatations. In consequence of the branching of the connective tissue basis, masses of it may be seen in transverse section apparently imbedded in the epithelium. Lying immediately on the connective tissue is a layer of somewhat columnar epithelial or epidermic cells, a layer which in this case is easily distinguished, as it takes on the carmine stain very readily. It corresponds to the germinal layer of the rete Malpighii or rete mucosum. Above this is a thicker and yellower layer, in which the cells are seen to have more formed material, and to be polygonal in shape, corresponding to the upper part of the rete Malpighii. Passing further outwards, a second deeply stained layer is reached—the stratum granulosum of Langerhans. Above this the stratum lucidum is not very distinctly seen under the low power, and the stratum corneum is represented by an exceedingly thin yellow streak.

Under the high power (× 300) examine the various tissues, the blood-vessels distended with blood, the fibro-cellular basis, in the young cells of which the nuclei undergoing division can frequently be seen. Then note the appearance of the columnar cells, with their deeply stained nuclei. Above this layer the cells become first irregularly round and then polygonal. About the level of the middle of this layer "prickle" cells are very well seen in this growth, and here the prickles may be seen passing into the body of the cell, in many cases appearing to be directly continuous with processes from the nucleus, though in some cases the nucleus is surrounded by a distinct vacuole. The processes of adjacent cells are continuous with one another, and may be seen to pass from nucleus to nucleus in all directions. The stratum granulosum is also very well developed; the cells of this layer are at the poles granular and deeply stained; but in the body of the cell there is a clear bright space. Each cell is more or less spindle-shaped. The stratum lucidum may be distinguished under

a high power, but it is never very well developed in the true papilloma, and in this form the stratum corneum is represented by a



FIG. 108.—Drawing of epithelium from the surface of a papilloma. Stained with picro-carmine. (× 300.)

a. Layer of flattened cells from near the surface of the rete Malpighii.
b. Well-formed prickle cells.
c. Vacuolated prickle cell.
d. Smaller rounded or polygonal cells, immediately above
e. The columnar or germinal layer.
g. Cellular connective tissue of papillary basis.

thin bright yellow band of horny squames only. In this tumour, as seen under the microscope, the distinguishing features are the enlargement and branching of the papillæ, the enormous development of the rete Malpighii and the stratum granulosum, and the thinness of the horny layer.

HORNY PAPILLOMA.

263. If a section of a horn be made, taken from the face or the neck, all the above features are repeated, with the exception of the last, and it will be found that the horny nature of the growth is due to an accumulation of the horny squames on the surface of the palpillomatous mass. Stained as in papilloma, the stratum corneum is seen as a dense yellow mass, which appears to fill up every crevice on the outer surface of the growth, forming a layer of very considerable thickness

over the stratum granulosum, which therefore does not stand out quite so prominently as in the ordinary papilloma. In order to understand this appearance the position of these growths must be remembered—face, neck, or in those positions from which there is secretion of a large quantity of sebaceous material. The horny layer, instead of being constantly shed, as from a normal cutaneous surface, or from the surface of an ordinary papilloma, is glued together by the large quantity of sebaceous material, and forms a kind of paste, which dries, hardens, and constitutes the smooth, horny mass as described.

Papillomas of the mucous membrane grow in the same way, but are covered by epithelium, similar to that which is normally present in the position from which they grow. These are the soft velvety growths which are met with in the bladder, intestine, and the rest.

Simple Adenoma.

264. The simple adenoma, of which that of the breast may be taken as the type, consists of a mass of gland structure, developing quite independently of that of the breast itself. It is a mass of glandular tissue growing from a separate centre, and is in no way connected with either the acini or the ducts of the mammary gland. Pathologists differ greatly as to the definition and nature of these tumours, and cystic sarcomas and primary cancers have been classed under this heading, but it will be well to distinguish the adenoma from the cancer in the same way as the papilloma is distinguished from the epithelioma, though in both cases, under certain conditions, the one may be followed by the others as a secondary growth. In speaking of the simple adenoma, it will be well to leave the consideration of the tubular adenoma to be taken up with that of the epithelioma.

In the true adenoma there is more than a mere increase in the amount of interglandular tissue or than a distention of the pre-existing ducts and acini. There is a true gland formation, accompanied in many cases by the growth of inter-acinous connective tissue, and also by a distention into cysts of the newly formed acini and tubules. Such tumours may vary very greatly in size, from that of a filbert to a growth many pounds in weight.

They are rounded or lobulated, and are surrounded each by a fibrous capsule, by which it is sharply defined from the surrounding tissue. Like most of the other simple tumours, it is of comparatively slow growth, and is not attached to the surrounding structures. There is no central umbilication, therefore no retraction of the nipple, as in the case of the scirrhous cancer, for which only it is liable to be mistaken. There are no secondary growths in the neighbourhood by implication of the glands.

To the naked eye it appears to be composed of a mass of fibrous tissue, sometimes containing cysts of various shapes and sizes in large numbers, in which is usually a quantity of opaque serous or gelatinous fluid.

In some cases the adenoma consists of a soft, pinkish mass, surrounded by a fibrous capsule.

Harden a piece of the tumour in Müller's fluid (§ 53, p. 42), and a second in methylated spirit (§ 52, p. 42); stain sections in picro-carmine (§ 73, p. 53) or logwood (§ 74, p. 56), and mount in Farrant's solution (§ 98, p. 71) or Canada balsam (§ 96, p. 69).

Under a low power (× 50) the tissue is seen to be composed of a regularly formed fibrous matrix, more or less cellular, according to the rapidity of the growth of the tumour. Running through the matrix are numerous blood-vessels. Supported by the fibrous tissue are tubes or acini in various stages of development, from solid columns of cubical epithelial cells to perfectly formed tubes, with distinct lumina or cysts of considerable size; at certain points may be noted the process of the opening out of the lumen from the solid mass of cells to the distinct cavity, surrounded by a layer of regularly arranged cylindrical or cubical cells.

For examination of the structure of this glandular tissue the high power (× 300) must be used. Examine the regularly developed fibrous stroma in which the blood-vessels are imbedded. Lying immediately on the fibrous stroma, and apparently taking the place of the basement membrane of the normal gland tissue, is a layer of delicate flattened cells, which may be spoken of as Debove's layer. Above this layer is usually only a single layer of columnar or cubical cells. Each cell has a distinct and well-formed nucleus; but in this form of tumour no cilia are met with. A somewhat deceptive appearance is

frequently presented, especially when the sections are not very thin. In some of the cavities it appears as though there were more than



FIG. 109.—Simple adenoma of the breast. Stained with logwood. (× 50.)

a. Column or double row of cells, of which the nuclei only are seen.
b. A more irregular mass or cylinder of cells.
c. Cyst formed by distention of an acinus or tubule.
d. Connective tissue basis.

even two rows of cells. Here it must be remembered that if the section is of moderate thickness, the knife, passing obliquely through the same layer of cells, exposes a somewhat elongated surface view, and so there is the appearance of several layers. Again, if the section be made through the epithelial lining of one side of the cyst, an apparently solid mass of epithelium is presented to view. It is very necessary to remember this in making an examination of adenomas.

The adenoma is developed in much the same way as is the mammary gland, for a description of which the student is referred to works on histology.

MULTIPLE, COMPOUND, OVARIAN CYSTIC TUMOUR (SYNONYMS—PROLIFEROUS OVARIAN CYSTIC TUMOUR; MULTILOCULAR OVARIAN TUMOUR).

265. The ovarian cystic tumour is a growth which, in its mode of development, simple nature and structure, may be compared to the

adenoma, and may be termed the adenoma of the ovary or of the peritoneum.

It may reach an enormous size, and it is then composed of a series of cysts, situated in the ovary or in the broad ligament. The tumour mass is encapsuled by a fibrous covering, and in the substance the cavities are bounded either by dense fibrous bands or spongy tissue, which, examined with a magnifying lens, is seen to be made up of a number of small cysts. The larger cysts usually contain a quantity of watery or serous fluid, in some cases almost like the fluid found in hydatid cysts, with common salt, but little albumen. This fluid may be variously coloured by altered blood pigment—purple, red, or yellow. The smaller cysts are filled with a gelatinous material, which is much more rarely blood-stained and contains more albumen.

For microscopic examination, the best is a small piece taken from the spongy tissue, in which minute glistening or gelatinous specks are seen.

Harden in Müller's fluid (§ 53, p. 42), cut sections (§ 67, p. 48), stain in picro-carmine (§ 73, p. 53), and mount in Farrant's solution (§ 98, p. 71), or stain in logwood (§ 74, p. 56), and mount in Canada balsam (§ 96, p. 69).

Examine under a low power (× 50). Throughout the section are numerous small cysts, imbedded in a somewhat cellular and highly vascular connective tissue. The nuclei of the connective tissue cells are deeply stained with the carmine, and stand out prominently. The blood-vessels are usually seen filled with the greenish blood corpuscles. The cysts are very irregular in outline; some are round or oval, and simple; others are subdivided by papilliform processes, pushing their way from the connective tissue stroma, and in some cases meeting in the centre, and dividing the primary cysts into smaller compartments.

Lining the cysts is a regular layer of epithelium, columnar and often ciliated, or excavated to form goblet or chalice cells. The nuclei of these cells can be distinctly seen, and are usually situated in the lower third of the cell, especially of the chalice cell. Notice that all the papillary projections are completely invested with a regular layer of epithelium.

Under the high power (× 300) examine the cellular stroma, with its numerous blood-vessels, and then the arrangement and appearance of the epithelial cells. There is no basement membrane; but, as in the adenoma of the breast, a layer of flattened nucleated cells is found between the columnar cells and the connective tissue—Debove's layer. From these flattened cells spring the cubical cells, which are

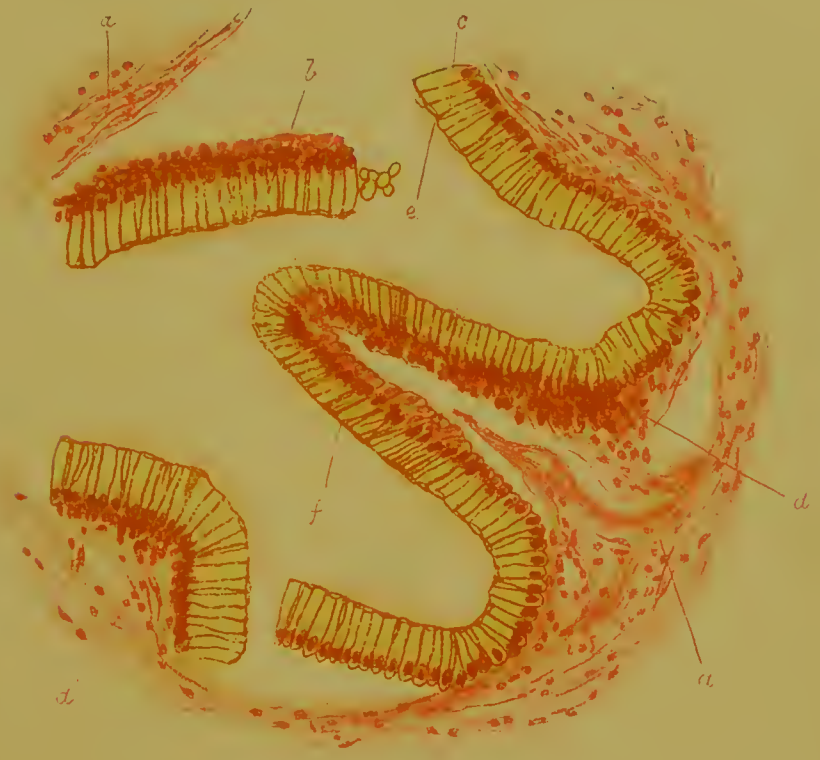


FIG. 110.—Drawing of section of a compound ovarian cystic tumour. Stained with picro-carmine. (× 300.)

a. Fibro-cellular connective tissue stroma.
b. Layer of flattened cells, or Debove's layer.
c. Single layer of chalice cells.
d. Several layers, of which the nuclei are seen.
e. Mouths of the chalice cells.
f. Mucoid material contained within the cyst.

arranged in a single or a double row. The deeper cells are more cubical than columnar, and interlock with the more superficial layer. The superficial cells are tall and columnar, a few of them are ciliated, but the greater number are chalice cells. The nucleus, as seen under the low power, is placed in the lower third of the cell. It is deeply stained, and stands out very prominently from the more delicately

stained cell. In the chalice cell the part above the nucleus bulges out slightly before the mouth of the cell is reached, which may be seen as an ovoid opening. The bulging part is more transparent than the lower third of the cell. Within the cyst a few cells are usually lying free, imbedded in a delicately tinted mucoid or colloid mass.

Cysts.

266. Cysts have been already described as present in the liver (§ 128, p. 125) and kidney (§ 168, p. 211), where they are due to the dilatation of obstructed ducts, to the accumulation of various epithelial or fluid materials, and to the distention of pre-existing cysts.

Other cysts have been described in the liver as due to the presence of parasites (hydatid cysts) or foreign bodies. Others again are formed by softening and degeneration in new growths, as in the case of the cystic myxoma (false cysts, or cysts of degeneration).

Cysts of new growth are also met with, as in the adenoma and the compound ovarian cystic tumour.

Peritoneal cysts are found as hydrocele and loculated peritoneal cysts, in which the peritoneum is prolonged into a small cavity or series of cavities separated from the main cavity, and then distended to form a cyst or cysts, in which case secondary cysts are budded off, as it were, from the primary sac and then distended.

Ranula.—The cyst which is found under the tongue in the frenum is a large cyst, lined with ciliated epithelium, and must be mentioned, as it was at one time thought to be merely a distended duct.

Endothelial cysts, such as bursæ, occur round tendons, and are caused by distention of their sheaths by exudation.

Distention of a closed cavity may give rise to a cyst formation, as in the case of goître, where, in certain circumstances, large cysts are found formed by distention of normal closed sacs of the thyroid gland, by a proliferation of the epithelium lining the cavity, followed by colloid degeneration of the cells, as in the case of the contents of colloid cysts derived from the renal epithelium.

One form of cystic tumour which deserves more than passing mention is the dermoid cyst. The tumour from which this description is taken was removed from the ovary, and was about the size of a

child's head at birth. It was firm at points, but on the surface a number of cysts projected. Some of these contained a quantity of glue-like fluid; others contained a soft fatty or sebaceous looking material; whilst others were filled with long hairs disposed in coils. When the mass was cut into, the knife "creaked" through nodules of cartilage, and then grated through calcareous or calcified patches. In the body of the tumour were larger cysts, though some parts of the growth were simply fleshy. Portions of the mass were hardened in Müller's fluid (§ 53, p. 42), and treated as for adenoma (§ 264, p. 408). On microscopic examination, under low (× 50) and high (× 300) powers, almost every tissue present in the human body could be distinguished—epithelium, squamous, evidently on a cutaneous surface; goblet cells, as from the intestine; ciliated, as from the trachea; hair follicles, with the deeply stained yellow hair in the centre, in transverse and longitudinal section; cartilage, with well developed capsules and matrix; muscular fibre, both non-striped and striped; blood-vessels in all stages of development; gland structures similar to those found in the bronchi, in the skin, and in the duodenum; small fragments of bone in process of calcification —in some parts the matrix pink, in others the peculiar green colour that picro-carmine gives with calcified structures; nerve fibres; multipolar nerve cells similar to those met with in the anterior horn of the cord; ganglion cells or large rounded cells with well-marked nuclei and long processes, such as are normally met with in the semilunar ganglia; masses of lymphoid tissue; fat globules; fibrous tissue, and tendon. The large cysts were all lined with ciliated or goblet-celled epithelium, except those into which hairs were growing, where most of the cells were more like ordinary cutaneous epithelium. This dermoid cyst, in fact, appears to be an attempt at the formation of a fœtus within the ovary itself.

Smaller and less complicated dermoid cysts are found in other positions, as the peritoneum and neck.

Sarcomas.

267. The sarcoma, as already defined, is a tumour composed of mesoblastic tissue in an imperfect state of development; but in conse

quence of the fact that there is always an attempt at the formation of some of the higher kinds of connective tissue there are many varieties of these tumours. The tumour may be simply a mass of granulation tissue, or there may be in the growth a partial formation of fibrous tissue, cartilage, bone, striped muscular fibre, &c.; and each of these tissues appearing in the tumour growth modifies to a certain extent the appearances, both naked eye and microscopic.

Small Round-Celled Sarcoma.

268. In the simplest form of sarcoma, the small round-celled form, occurs the most elementary type of connective tissue, the typical sarcomatous structure.

To the naked eye it presents a very characteristic appearance. It occurs especially in the fasciæ and in the loose areolar tissues, in the subcutaneous tissues, in the connective tissue of the nerve centres, retina, bones, muscles, testicle, and mamma, as a primary growth; but it does not affect the lymphatic structures. As a secondary growth it almost invariably first makes its appearance in the lungs, after which it affects specially the more vascular organs, in which there is a complex capillary system. It is a very soft, in some cases almost pulpy, tumour, or is like a piece of brain tissue. It is usually rounded, grows rapidly, and to the naked eye is sharply defined from the surrounding healthy tissue. In colour it is pale pink, and, unlike most of the tumours hitherto examined, has no glistening white fibrous streaks running through its substance, but yellowish or creamy patches—due to fatty degenerative changes—are frequently observed on the surface of a section. Still more characteristic are the small red, brown, and yellow points which occur in almost every sarcoma of this group—hæmorrhagic patches in various stages of alteration. Hæmorrhages are common in all forms of sarcoma, but especially in the small round-celled form, and in the myeloid sarcoma, to be afterwards described.

Harden a piece of the tumour in Müller's fluid (§ 53, p. 42), in order to keep as much blood in the tissue as possible; cut sections (§ 67, p. 48), stain one in picro-carmine (§ 73, p. 53), and mount in Farrant's solution (§ 98, p. 71), a second in logwood (§ 74, p. 56) and Canada balsam (§ 96, p. 69).

Under the low power (× 50) a mass of small round cells may be observed gradually invading or infiltrating the surrounding tissues, especially along the lines of connective tissue, and thus in a sarcoma growing in muscle the fibres and fibrils are gradually separated by the infiltrating small round cells. Where the tumour tissue is very distinct, a series of lines of elongated cells may be distinguished, usually arranged in double rows, and between these double rows of elongated cells greenish lines may be seen. These are the embryonic blood-vessels, and the green granular lines are the strings of coloured blood corpuscles. The great resemblance of this mass to granulation tissue will be at once recognised.

Examine under a high power (× 300, or better, × 450). Here the elementary cell structure is much more easily distinguished. The majority of the cells are from $\frac{1}{2500}$ to $\frac{1}{1000}$ inch in diameter (all larger than the coloured blood corpuscle, which is about $\frac{1}{3200}$ inch). There is no cell wall, but within each of these cells is a distinct deeply stained nucleus, $\frac{1}{3000}$ to $\frac{1}{2500}$ inch in diameter; and within the nucleus again nucleoli are to be observed as deep crimson dots. Between the cells is a very small quantity of granular homogeneous intercellular substance, which in many cases is discernible with great difficulty. The elongated cells must also be observed under this power. They are seen to be only sarcoma cells which have

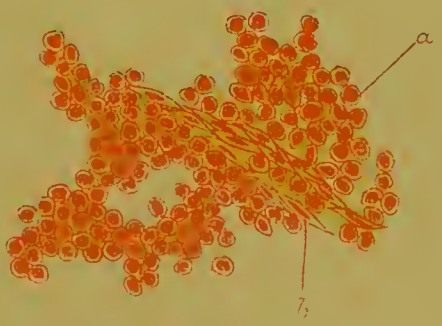


FIG. 111.—Small round-celled sarcoma. Stained with picro-carmine. (× 300.)

a. Small round cells, with large nuclei and well-marked nucleoli.
b. Flattened spindle-shaped cells, forming the walls of the embryonic blood-vessels.

taken their present shape because of the pressure to which they have been subjected, and the blood corpuscles which lie between the rows of elongated cells appear to have been the compressing agents,

and it appears as though the blood had simply been forced in between the sarcoma cells. The blood-vessels in this growth are quite embryonic in type, and are composed of modified sarcoma cells only. Examine a transverse section of such a vessel, and note the flattened layer of cells next to the blood current, and then the gradual transition from the flattened to the rounded cell in successive layers. In connection with this structure must be remembered the occurrence of the small hæmorrhages, and the method of spreading of the tumour. The walls of the vessels in the tumour are exceedingly delicate, and the least extra strain on them causes them to give way, when blood is poured into the surrounding sarcomatous tissue. This can be seen even with the naked eye, and may be corroborated under the microscope. The tumour cells are in direct contact with the blood current, and some of them may be carried by the blood, first to the lungs, where secondary growths first make their appearance, and then to the other organs, especially those of great vascularity. The small round-celled sarcoma is perhaps the most malignant of the group. It grows exceedingly rapidly, infiltrates locally, and spreads by the blood-vessels. The degenerations to which it is liable will perhaps be best considered with those of the other sarcomas.

Large Round-Celled Sarcoma.

269. The large round-celled sarcoma must be mentioned here. It differs very markedly, in many respects, from the preceding form. It grows in much the same positions, but affects specially the submucous tissue of the pharynx and posterior nares, where it forms a firm, almost fibrous, pale, polypoid growth, much smaller and more sharply defined from the surrounding healthy tissues. It is to a certain extent malignant, but in a much lower degree than the small round-celled sarcoma, and rarely gives rise to secondary growths.

Harden in Müller's fluid (§ 53, p. 42), stain in picro-carmine (§ 73, p. 53), mount in Farrant's solution (§ 98, p. 71); or stain in logwood (§ 74, p. 56) and mount in Canada balsam (§ 96, p. 69).

Examine under low (× 50) and high (× 300) powers, first the cells which are seen to be rounded, and some two or three times

as large as the cell of the smalled round-celled form. Within these cells are two, three, or four large ovoid nuclei, surrounded by a quantity of protoplasm. Throughout the tumour is a delicate fibrillated intercellular substance, which at certain points is collected into thicker bands. These, along with thin walled vessels, divide the large cells into groups, which vary in size. At other points, especially where the fibrillar tissue is present in large quantity, elongated or spindle cells may be seen, almost like those which are found in organising granulation tissue. The vessels, as in all sarcomas, are quite embryonic in type, and have thin cellular walls.

Spindle-Celled Sarcoma.

In the spindle-celled sarcoma there is an attempt at the formation of more highly organised connective tissue. The cells become elongated, and in most cases the amount of intercellular substance is increased, and the development of the vessels is a little more advanced.

Of these tumours the more important are the following.

Recurrent Fibroid Tumour.

270. The recurrent fibroid of Paget, like the other tumours of this group, is found growing from connective tissue in almost any position, but especially in fasciæ, periosteum, breast, kidney, liver, skin, and dura mater. The cases recorded by Paget appear to grow principally from periosteum and subcutaneous tissue in various parts of the body. They vary in size from that of a filbert to as much as a foot in one of their dimensions, and are characterised by their tendency to recur locally, but without any special tendency to local infiltration. They are rounded or lobulated, and are firmly attached to the tissue from which they grow. On section they are firm, tough, and irregular, and have frequently a fleshy look. They may be pale pink or brownish red, almost like the fibroma, and the surface has a streaky look, as if from the presence of bands of fibrous tissue. It is from this appearance that they get the name "fasciculated sarcoma."

Harden in Müller's fluid (§ 53, p. 42), stain in picro-carmine (§ 73, p. 53), and mount in Farrant's solution (§ 98, p. 71).

Examine under a low power (× 50), for the fasciculated appearance. A series of bundles of cells may be seen interlacing with one another in all directions ; so that some are cut longitudinally, others obliquely, others again transversely. In the tissue few blood-vessels are found, and such as are present are of higher organisation than are those found in the small round-celled sarcoma.

Under the high power (× 400) the bundles are seen to be made up of "narrow, spindle-shaped, elongated, caudate, and oat-shaped nucleated cells." In these cells are nuclei, which are said to distend the body of the cell at the point at which they are present. Some of the cells are bifurcated at the ends, but the majority of them are oat-shaped. Between these cells is a small quantity of fibrillated intercellular substance. These tumours recur locally only when they are imperfectly removed, and in the first instance do not give rise to secondary growths ; but when they have been repeatedly removed, the recurrent mass very frequently resembles much more nearly the form next to be described. It becomes more sarcomatous in its nature.

True Small Spindle-Celled Sarcoma.

271. This grows in much the same positions as the foregoing, and, like it, comparatively rarely gives rise to secondary growths. It is surrounded by a more or less definite capsule, and on section presents a firm, solid, or elastic, pale, fleshy looking surface ; not so smooth as the oat-shaped form, and with the glistening or fibrous looking streaks more pronounced. The mass may reach a very considerable size ; and when secondary growths do occur, they are found in the same position (the lung first) as the other sarcomatous growths.

Prepare as before, and examine under both low (× 50) and high (× 400) powers. The spindle cells are more perfectly formed, and, as a rule, are somewhat larger and more elongated than are the cells of the recurrent fibroid proper. They are arranged in bundles, which interlace in all directions, so that the cells are seen in various sections. Those cut longitudinally are seen as the ordinary spindle cells, with ovoid, or, in some cases, rod-shaped nuclei. Others are cut obliquely, and these appear to be ovoid cells ; whilst others again, cut transversely, appear to be round cells. It must be noticed,

however, that these sections are comparatively small, and that some of them have no nucleus, owing to the fact that the sections are made near the end of the cells to which the ovoid nuclei do not extend.

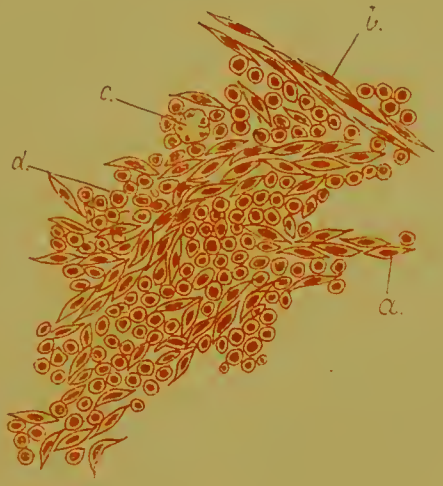


FIG. 112.—Small spindle-celled sarcoma. Stained with picro-carmine. (×300.)

a. Well-formed spindle cells.
b. More elongated spindles bounding one of the vascular channels.
c. Embryonic blood-vessel cut transversely.
d. Transverse section of spindle cell. (This transverse section, with the section of the nucleus in its centre, must not be mistaken for a round cell.)

Where the section passes transversely through the centre of cell, the nucleus, of course, is divided, and the rounded section appears to have a nucleus also.

Running through the section embryonic blood-vessels are found, similar in structure to those met with in the small round-celled sarcoma; but here they are not so numerous.

MYELOID SARCOMA.

272. The myeloid or giant-celled sarcoma is perhaps the most common form in which the small spindle-celled sarcoma is found. It consists of a small spindle-celled sarcoma with the addition of giant cells, these being present probably because of the position in which the tumour occurs.

They are large tumours, of slow growth, occurring either within the shaft or epiphyses of a bone or under the periosteum, especially in the

following positions :—the upper end of the tibia, the lower end of the femur, upper end of the humerus, on the outer surface, or within the lower jaw, constituting one form of malignant epulis, or in the antrum. When growing under the periosteum they are surrounded by a fibrous capsule only; but when in the centre of the bone they expand the outer shell, which may become so thin that it crackles under the finger. They are moderately firm, fleshy, or elastic, pinkish or brownish yellow in colour, and on section have a peculiar "fasciculated" or sometimes a marbled appearance. The peripheral or growing part of the tumour is usually more pink than the centre, which is pale or brownish yellow, almost fatty looking, and variegated with patches of brown or red (hæmorrhages of various ages), whilst at certain points are cysts containing a yellow or brown gelatinous material (derived from softened tumour tissue stained with altered blood pigment). On section small fragments of bone may be found, especially near the periphery of the tumour. The hæmorrhages and cysts are very characteristic of this form of growth, as the vessels are numerous, embryonic in structure, and situated in a tumour which is especially liable to injury from external violence, from its exposed position and the unyielding structure on or in which it grows.

Treat as for recurrent fibroid tumour (§ 270, p. 417). Under the low power, the bundles of small spindle cells, well developed, and cut in various directions, are readily observed. Throughout the mass small green granular masses are seen (small collections of coloured blood corpuscles), and then the giant cells, more or less numerous, are seen as masses of protoplasm, delicately stained, with small crimson specks scattered through them. Under this power they appear to be about the size of a pin's head. The delicate green lines indicating the position of the blood-vessels are very numerous; and in a specimen hardened in Müller's fluid they are much more readily distinguished than in one hardened in spirit.

Under the high power (× 300) examine the spindle cells. The description given of them in the spindle-celled sarcoma applies in this case also. The blood-vessels are exceedingly numerous, and are composed simply of tumour cells, more or less regularly arranged in rows, between which the coloured blood corpuscles (green) have pushed

their way. Around these embryonic blood-vessels green masses of extravasated blood are frequently met with, the corpuscles, with their double outlines, lying in direct contact with both spindle-shaped and giant cells.

The giant or myeloid cells resemble very closely the osteoclasts of bone. They are large irregular masses of delicately tinted proto-

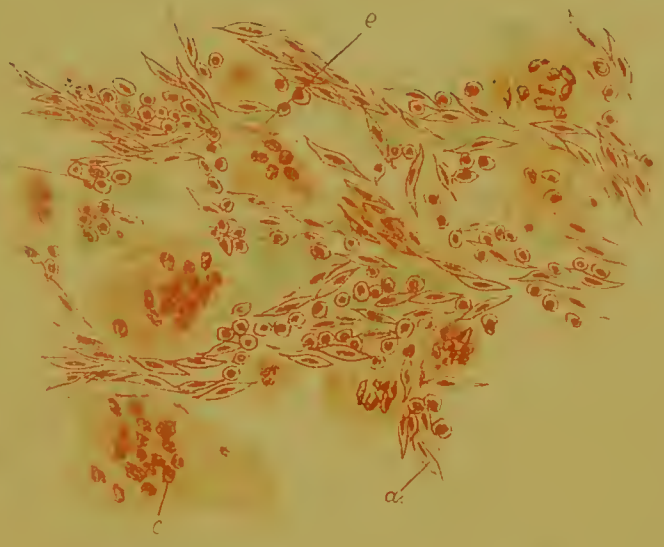


FIG. 113.—Myeloid or giant-celled sarcoma. Stained with picro-carmine. (× 300.)

a. Spindle cells, of which the tumour is principally composed.
b. Cells arranged to form the walls of embryonic blood-vessels.
c. Giant cell, with large number of nuclei scattered throughout its protoplasm.
d. Transverse sections of spindle cells.
e. Extravasated coloured blood corpuscles escaped from ruptured vessels.

plasm, in which are imbedded twelve, twenty, or more deeply stained nuclei scattered irregularly throughout the mass. In many cases these cells are also vacuolated.

Although this is the typical form of the giant-celled sarcoma, it must be remembered that these giant cells may be met with in any sarcoma which is growing in connection with bone, so that their presence must be looked upon simply as an accident of position of the tumour. Granules of altered blood pigment may usually be seen in this tumour, and in the yellow patches especially many of the spindle cells are becoming granular and fatty, so that the myeloid, like the round-celled, sarcomas frequently become fattily degenerated.

The typical form seldom gives rise to secondary growths; but such secondary tumours as have been examined are found in the position ordinarily affected (the lung), and then they contained no giant cells, but were simply small spindle-celled sarcomas.

Large Spindle-Celled Sarcoma.

273. This tumour is not absolutely distinct from the small spindle-celled sarcoma, but it differs in many respects, both clinically and pathologically, from that form. Although it seldom reaches such a large size, its growth may be much more rapid, it infects locally, and gives rise to secondary growths at a comparatively early stage. The primary tumour occurs in the same position as the other forms of sarcoma, but it is found especially in the skin, from which the lymphatic glands are frequently affected, followed rapidly by secondary growths in other glands, the lungs, liver, intestine, brain, pleura, pericardium. To the naked eye they appear to be softer, more pink, and more vascular than the small spindle-celled form, and hæmorrhagic patches and soft gelatinous cysts similar to those found in the myeloid sarcoma are of frequent occurrence.

Prepare as for the recurrent fibroid (§ 270, p. 417), and examine under low (× 50), and high (× 300) powers. The cells are considerably larger (three or four times) than those of the small spindle-celled sarcoma. They are more like the ordinary fibro-plastic cells, but have between them little or no intercellular substance or periplast. They are very irregular in shape, are frequently bifurcated, and are arranged in bundles, the cells interlocking by their bifurcated ends. The blood channels between these cells are very numerous and of embryonic structure, and green masses of extravasated blood are pretty frequently seen. As some of the bundles are cut transversely, rounded sections, some nucleated, others without nuclei, are scattered over the field.

Melanotic Sarcoma.

274. The most important of the large spindle-celled sarcomas is the melanotic sarcoma, which grows especially from the choroid coat of the eye, the skin, and the pia mater. The specimen of which a

description is here given was a large fungating blue-black mass, projecting from the orbit, and growing from the choroid through the eyeball at the upper margin of the cornea. It measured about two and a half inches in diameter, and bled on the slightest touch. On section, the mass was deep brownish or blue-black at certain parts; in other regions it is slaty grey, whilst in areas it is white or pale pink. It is comparatively soft, and is extremely vascular. Prepare as at § 270, p. 417, and examine under a low power (× 50). Under this power note the arrangement of the large spindle cells into an open

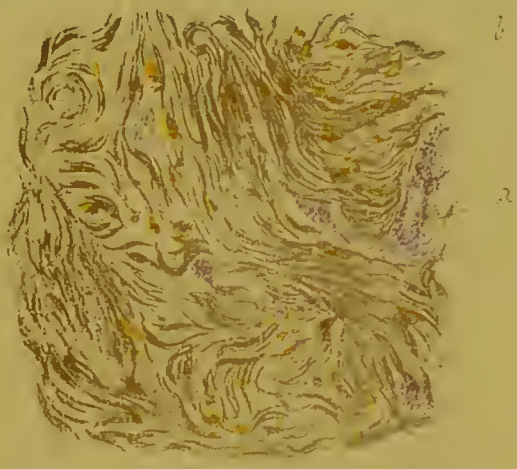


FIG. 114.—Drawing of melanotic sarcoma. Stained with logwood, and mounted in Canada balsam. (× 60.)

a. Small deeply stained cells.
b. Spindle cells, with protoplasm around the nucleus deeply pigmented.
c. Large spindle cells, arranged concentrically.
d. Large non-pigmented spindle-shaped or irregular cells.
Notice the peculiar concentric and reticular arrangement of these cells.

concentric network, with, in some cases, numerous small round cells lying in the meshes. Remember also that some of the large cells are cut transversely, and that they are frequently arranged in bundles. At certain points only pigment may be seen collected, chiefly around the nuclei of the large spindle cells.

Under the high power (× 300) examine the large spindle-shaped or branching cells of which the open network is composed, examine both longitudinal and rounded transverse sections, and also the great number of small round cells with which, in some cases, the meshes

are crammed. Notice the embryonic blood-vessels, with tissue which presents all the characters of lymphatic tissue around them. Around some of these vessels, also, are found small hæmorrhages, in which there is a collection of altered blood pigment. This altered blood pigment must be carefully distinguished from the melanin proper, which is found in cells of the tumour. The melanin, or black pigment of the tumour, is not directly derived from the blood pigment, but appears to be elaborated by the large cells of which the tumour is composed. Under a high magnifying power it is seen as golden yellow or black granules, situated around the nuclei of the large spindle cells, more rarely in their protoplasm, and more rarely still in

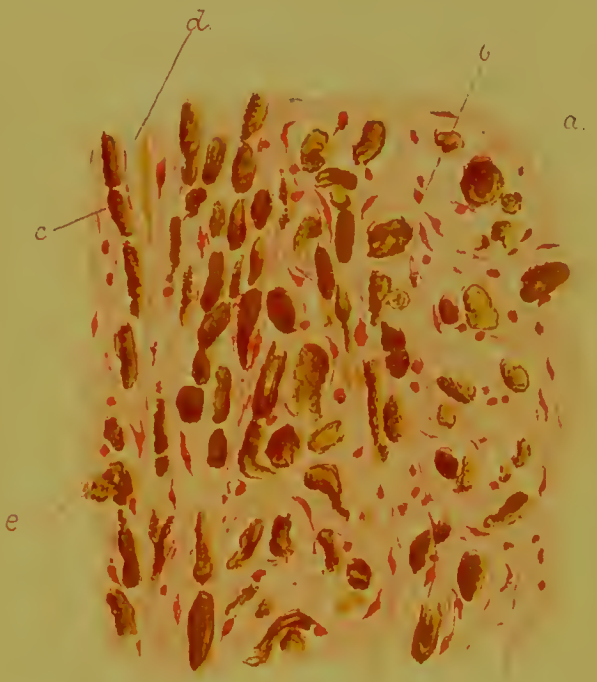


FIG. 115.—Melanotic sarcoma. Stained with carmine, and mounted in Canada balsam. (× 450.)

a. Round cell distended, with golden brown pigment.
b. Delicate fibro-cellular tissue between the pigmented cells. Notice the peculiar arrangement of the fibres.
c. Spindle cell distended with pigment.
d. Granules of pigment lying around the nucleus of a smaller spindle cell.
e. Pigment distributed around the cell.

the spaces between the cells; treated with dilute hydrochloric acid, and then soaked in a solution of potassium ferrocyanide, no blue reaction is obtained; but if a section be boiled in a solution of caustic potash, the pigment is dissolved, and a brown tinge is given to the

caustic potash solution, which immediately disappears on the addition of chlorine water. The pigment seen in old hæmorrhages, in brown induration of the lung, &c.—gives a blue reaction with hydrochloric acid and potassium ferrocyanide, whilst the coal pigment found in the lung gives no blue reaction, and is perfectly insoluble in boiling caustic potash.

This is an extremely malignant form of tumour, and secondary growths usually make their appearance whenever the primary growth has reached the size of a walnut. These secondary tumours may make their appearance in any of the positions above mentioned, and they are frequently deeply pigmented, though in some cases they are entirely devoid of colouring matter.

(For appearance of secondary growth, see § 207, p. 300). They are specially malignant, as they extend not only locally and by blood-vessels, but also by the lymphatics. They appear to be most malignant when growing from the true skin, and secondary growths may be looked for in all positions above mentioned, and in the liver, submucous tissue of the intestine, and the rest, where the primary growth has reached the size of a marble.

It must be remembered in connection with these sarcomas that various modifications may occur, and that all varieties of combinations of the cells, in form, number, and arrangement, are found, and all sarcomas therefore will not present the regular or typical appearances above represented. Where the mixed sarcomas occur, they are usually locally and generally malignant, and most frequently have a tendency to attempt the formation of some more highly developed tissue.

Alveolar Sarcoma.

275. The alveolar sarcoma first described by Billroth is a form of tumour which grows most frequently on the true skin, and in the pia mater, muscle, and bone. They grow as small tumours, which have most of the characteristics of the ordinary sarcoma. (Treat as for recurrent fibroid tumour.)

Under the microscope, this tumour at first sight very much resembles a carcinoma. The cells are of considerable size, and are

almost epithelial in character. They are large, rounded, may have a couple of nuclei, and each nucleus has several deeply stained nucleoli. In consequence of the arrangement of pre-existing and newly formed vessels, these cells are divided into groups. Along with the blood-vessels is a quantity of fibrillar tissue, which extends in some cases in delicate strands between individual cells, "but no vessels enter the cell groups."—(Ziegler.) From the description given by various authors, and from the examination of a single specimen, the tumour appears to be formed from lymphomatous tissue, in which the proliferation of the endothelial or endothelioid cells takes place rapidly without a corresponding increase in the amount of stroma, the vessels and reticulum forming the thicker bands and more delicate stroma between the groups of cells. The vessels are increased in number at the same time as the endothelioid cells proliferate. Ziegler describes a similar process taking place in the tissues of the sub-arachnoid space and pia mater, where, he says, the masses of cells are formed from the endothelial covering of the trabeculæ, the cells proliferating and forming thicker and thicker investing layers until the spaces are completely filled. This growth might be described as a lymphadenoma, with but a small formation of fibrillar tissue, in which sense it is an endothelioma and a true sarcoma.

An *angio-sarcoma* is a pulsatile tumour, in which the whole mass appears to be converted into embryonic blood-vessels. The process of development of blood-vessels is exactly similar to that already described in other sarcomas, but is carried to a greater extent.

Psammoma or Angiolithic Sarcoma.

276. This tumour derives its peculiarities from its position as an outgrowth of the fringes of the choroid plexus or the pineal gland. It consists of a mass of spindle cells, with a large number of blood-vessels. Growing in or from this sarcomatous mass are a number of bud-like or club-shaped processes, which appear at the sides of the vessels. The vessels themselves are surrounded by layers of spindle cells, or flattened cells seen in section, which are prolonged on to the outer surface of the bud. The centre of the bud is occupied by a hard, often cretaceous or colloid mass, either single or composed of

several pieces, very like the ordinary brain sand. In some cases similar growths appear, which are, however, covered by more fully formed connective tissue; in which case they are undoubtedly non-malignant, though in the first form local infiltration of the surrounding tissues has been described.

Osteo-Sarcoma.

277. In the osteo-sarcoma, properly so called, there is the formation of bony spicules, not only in the primary but also in the secondary growths. These tumours vary very much as regards the size and shape of the cells of which they are built up, but in all cases they grow primarily in connection with bone. They grow first as ordinary sarcomas, and present all the appearances already described. They are malignant, and multiple tumours soon make their appearance, as on the ribs, where the characters of the primary growths are repeated.

On cutting into the tumour small hard spicules are met with; but as they are principally composed of a cancellous form of bone, they



Fig. 116.—Osteo-sarcoma stained with picro-carmine. (× 80.)
a. Band of old fibrous tissue.
b. Sarcoma cells.
c. Pink bony matrix, as yet apparently fibrous.
d. Cells lying in the fibrous matrix.

may be cut through with a knife. Prepare as for the other sarcomas (§ 270, p. 417), and examine under the low power (× 50). The

softer parts are composed entirely of cells, round or spindle, as the case may be. At certain points pink bands of fibrous looking tissue may be seen pushing their way between the masses of cells (the matrix is becoming fibrous.) Passing further, in the same direction, small green patches come into view, in which may be seen regular bone structure. In these patches or spicules there is the regular lamination. Haversian canals may be distinguished, and all the essential features of true ossification.

Under the high power (× 300) it will be seen that the tumour cells take the place of the osteoblasts in this bone, but that otherwise the spicules are in all respects like true cancellous bone. Further, it must be noticed that in the neighbourhood of these growing centres of ossification the cells are modified, many have assumed the characters of cartilage cells imbedded in spaces bounded by capsules, and surrounded by the pink matrix. Later these seem to become impregnated with lime salts, just as in the growth and development of normal bone.

Osteoid-Sarcoma.

278. A very malignant form of sarcomatous tumour is the osteoid sarcoma, which grows primarily from the periosteum, but which gives rise to secondary growths in the lungs, serous membranes, and other organs. Prepare as above (§ 270, p. 417). Examine under the low power, and note that there is an increase of the intercellular substance, and that the cells are considerably larger than those of a small round-celled sarcoma, and are multinucleated.

Under the high power (× 300) examine more carefully the large rounded multinucleated cells, between which is the translucent intercellular substance, delicately stained with the carmine of the picro-carmine; whilst at certain points, especially near the newly formed blood-vessels, this material is infiltrated with dark or highly refractile calcareous particles. Where the calcification is complete, the section gives a green reaction with the picric acid of the picro-carmine. The true bone structure is entirely wanting in this tumour, and the hardness, from which the tumour derives its name, is due entirely to the calcification of the cartilaginoid matrix.

Degenerations and Modifications of Structure of Sarcomas.

279. These sarcomas may undergo fatty degeneration of the cells, which become granular, and finally may break up entirely. This is readily recognised, even with the naked eye, as patches of the tissue become cream coloured or yellow.

Hæmorrhagic degeneration from rupture of the embryonic blood-vessels is also very frequently met with. This is often accompanied by the so-called cystic degeneration, as described in the myeloid sarcoma (§ 272, p. 420).

Hyaline degeneration, especially of the cells in the immediate neighbourhood of the blood-vessels, forming a kind of hyaline covering for the vessel, occurs.

Myxomatous degeneration of sarcomatous cells is also often found. The tumour then becomes mucoid, and, on microscopic examination, clear mucoid globules are seen in the swollen cells. This must be carefully distinguished from mucoid softening of the intercellular substance.

The following are modifications of structure rather than true degenerations :—Fatty infiltration of the sarcoma cells (lipomatous sarcoma); pigmentation of the cells, as in melanotic sarcoma.

Myxomatous softening, calcification or chondrification of the intercellular substance, as in the forms of sarcoma above described.

Epithelial Tumours.

280. For convenience of description, the epithelial tumours may be grouped together as belonging to the third class, in which there is "growth of some or all tissue elements in excessive and erratic forms, in which there is great vegetative power, the members of which are highly parasitic and malignant, infecting locally by direct transport, and through lymphatics and blood-vessels. Secondary growths may affect any tissue."—(Greenfield.)

From the definition it will be at once understood that these tumours grow from the mesoblast, but involve at the same time epi- or hypoblast tissues. A definition of one will cover, to a certain extent, the whole group; but there are slight modifications of structures in different species.

Epithelioma.

The first of the epithelial tumours to be considered is the epithelioma proper, in which the principal factor is an excessive overgrowth of epithelium, which invades the subjacent tissues by the lymphatic system, and produces secondary growths in the lymphatic glands and other parts.

These are divided into two classes, according as they originate :—(1.) on a surface covered with squamous epithelium—the squamous epithelioma; or (2.) from a surface covered with columnar or cubical epithelium—the columnar epithelioma.

(1.) Squamous Epithelioma.

281. This occurs usually at the points of junction of the skin and mucous membrane, or at those parts which from their movement and position are exposed to considerable irritation; where, too, the epithelium is in a state of great proliferative activity—the lips, tongue, mouth, orifice of vagina, rectum, and penis. The fully developed epithelioma occurs as an irregular warty looking mass, the surface of which is ulcerated, and has an extremely characteristic appearance, generally compared to that of a cauliflower, from the prominence of certain small white points and ridges, and from this surface exudes an irritant watery or ichorous fluid. The ulceration is in the main mass only, which is more or less rounded. At the margin of this large mass there is extreme induration, whilst surrounding it, but at some little distance, are numerous small firm nodules, each of which has a distinct boundary. On scraping the surface with a knife, the small white points come away as rounded pellets, leaving behind them distinct pits or depressions. Press one of these between two glass slips, and then examine in neutral solution (§ 34, p. 32), when it is found to consist principally of large flattened epidermic scales, which stain yellow with picro-carmine.

On section the tumour is firm, and running through the mass, especially bounding the white or yellowish masses of epithelium, are white glistening fibrous bands; but there are very few blood-vessels, as one would expect, from the fact that hæmorrhages are extremely rare from epitheliomatous surfaces.

Harden portions of the tumour in picric acid (§ 61, p. 45), in Müller's fluid (§ 53, p. 42), and in methylated spirit (§ 52, p. 42). Stain one section in picro-carmine (§ 73, p. 53), and mount in Farrant's solution (§ 98, p. 71); a second in logwood (§ 74, p. 56), and mount in Canada balsam (§ 96, p. 69).

Under the low power (× 50), examine first the free surface of the tumour, especially near the margin, where there will at once be noticed an extraordinary development of squamous epithelium; the masses, instead of merely clothing the papillæ, become enormously enlarged, extend for some distance into the subjacent tissues, and send out secondary finger-like processes in all directions. Around these hypertrophied masses of epithelium there appears to be a considerable increase in the number of small round cells in the connective tissue, and although the vessels do not come near the surface, because of the thick layer of epithelium, in this subjacent tissue they are often of considerable size. In the still deeper tissues the masses of epithelium (stained brown) are seen running in all directions, each mass being surrounded by the cellular proliferating con-

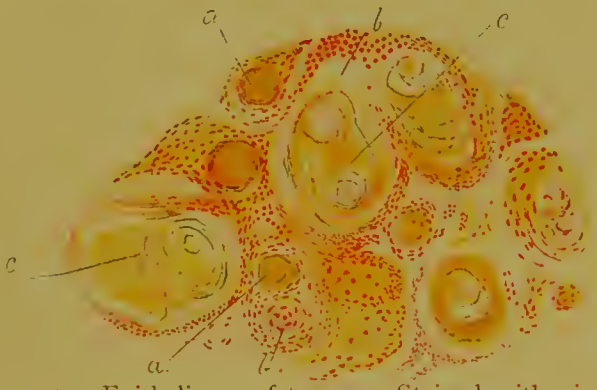


FIG. 117.—Epithelioma of tongue. Stained with picro-carmine. (× 100.)

a. Colloid centres of epithelial globules or "cell nests."
b. Flattened layers of cells around these colloid centres.
c. Larger colloid masses. These colloid masses are probably composed partly of horny squames, such as are met with, as the stratum corneum of the normal skin.

nective tissue (stained pink). At certain points in these brown masses of epithelium are yellow masses, evidently composed of strata or layers of flattened cells, the centre of the mass being almost homogeneous. These yellow masses are the cell nests which are so characteristic of the epithelioma.

Under the high power (× 300) observe that the epithelial cells of which the penetrating columns are composed are in all respects like those which are found on a cutaneous surface. The rete Malpighii and stratum corneum can be readily distinguished, and it is to this fact that the tumour owes its characteristic appearance, especially near the surface. The rete Malpighii is usually very well marked ; the germinal layer and the prickle cells are also easily distinguished. The



FIG. 118.—Diagramatic sketch to represent the changes which take place during the invasion of connective tissue by epithelial columns.

s.c.	Stratum corneum or horny layer of the cuticle.
s.l.	Stratum lucidum.
s.gr.	Stratum granulosum.
R.M.	Rete Malpighii—*b*. Superficial more flattened cells, beneath which are the well-formed prickle cells. *a*. Layer of columnar or germinal cells.
c.	Epithelium at normal level.
d. and *e.*	Epithelial bands passing downwards between the papillæ.
f.	Normal connective tissue papilla.
g.	More cellular and vascular connective tissue.
v.	Blood-vessels.

stratum granulosum and stratum lucidum are not so readily made out, but the horny layer is frequently very highly developed, especially

in the cell nests, which under this power are seen to be composed of concentric layers of flattened cells arranged around a central colloid mass. In order to understand the method of formation, it must be remembered that, as in the normal skin, the epithelial cells are removed from the germinal layer, they gradually become dry, horny, and flattened, losing their nuclei; they then form the horny layer, and are shed. In the pits into which the epithelium grows, in the epithelioma, as the cells are removed from the germinal layer on the walls of the pit they are carried to the centre of the "shaft," and there, as they cannot be removed as on a free surface, they undergo horny or colloid changes, and form a hard centre or core against which succeeding layers of cells are projected and flattened, and in this way arises the peculiar lamination to which reference has been made.

Notice that near the surface, or where the epithelial projections have passed in for no great distance, there are few round cells in the connective tissue, but that where the prolongations have passed further into the lymphatic spaces, the round cells become more numerous, and the vascularity of this tissue in such cases may become greatly increased. In the secondary growths the epithelial masses are usually growing more rapidly, have prickle cells well developed, no horny layer, and are surrounded by more of the round-celled tissue.

This form of tumour grows slowly, and is not very malignant. When secondary growths occur, they are found first in the lymphatic glands, where they frequently cause superficial ulceration, after which they may be found in almost any position.

It must be distinguished from papilloma by the fact that the epithelium, in place of remaining in its normal relation to the subjacent corium and connective tissue, invades these structures by the lymphatic spaces, and when this occurs malignity sets in. They spread or give rise to secondary growths, through the medium of the lymphatics, as is the case with all the cancerous tumours, and where once the invasion of the lymph spaces has commenced, the vegetative power of the epithelial growth rapidly increases.

The varieties of this form of epithelioma are due almost entirely to the rate of growth and position of the tumour; it is therefore unnecessary to enter into any detailed account of them, but it must be

remembered that where the tumours are of slowest growth, the cell nests are most perfectly formed, and that where the growth of the epithelial columns is very rapid, the cell nests may be absent, especially in the case of secondary growths.

(2.) Columnar-Celled Epithelioma.

282. The columnar-celled epithelioma is also termed, with almost equal accuracy, the malignant adenoma, or adenoid cancer, for in structure it is found to occupy an intermediate position between the simple adenoma and the true cancer, and also to bear the same relation to a papilloma of the intestine that a squamous epithelioma bears to the cutaneous papilloma.

It may be considered that the invading epithelium, in place of being squamous, is columnar or cubical, that processes branch or bud, and project into the subjacent tissue, where they give rise to spaces which are lined by a distinct layer of columnar epithelium, that this epithelium in some cases proliferates, and becomes more or less irregular. Sections of such a tumour have very much the appearance of a true cancer of the encephaloid type. Between the epithelial prolongations a variable amount of fibro-cellular connective tissue is formed, which appears to be the result of an irritative overgrowth of the pre-existing connective tissue.

If a structure similar to that already described is met with especially as a primary growth in the large intestine, sigmoid flexure, and rectum, as a soft, pale, succulent mass projecting into the intestinal tube. The surface frequently ulcerates in this position. It is so frequently met with in the lower part of the bowel, that it is spoken of as the malignant polypus of the rectum. It is also met with in the stomach in a flatter form, where it is liable to undergo a peculiar softening, almost like that of colloid cancer, for which it may easily be mistaken; in the liver, commencing in the epithelium of the bile ducts; and in the lungs, probably from the epithelial layer of the bronchial glands.

In the liver this columnar-celled epithelioma presents to the naked eye very much the appearances of true cancer. Scattered throughout the substance of the organ are a number of rounded or irregular masses, each of which has a characteristic appearance, the growing or

peripheral part is much more vascular, softer, and more pink than the centre, where the tissue is much yellower, and in some cases even fibrous. These masses, therefore, very closely resemble scirrhous cancer in an early stage of development.

In sections taken from the rectum, the liver, and the lung, the tumour structure may be easily determined.

Harden in Müller's fluid and spirit (§ 54, p. 43), stain one section in logwood (§ 74, p. 56), and mount in Canada balsam (§ 96, p. 69); stain the others in picro-carmine (§ 73, p. 53), and mount in Farrant's solution (§ 98, p. 71).

Under the low power (× 50).—In the purest form, as seen in the rectum, there first appears to be an enormous increase in the size of the gland tubes in the true mucous membrane. From this point there is a gradual invasion of the deeper structures until the whole thickness of the intestinal wall is involved. Between the large gland-like tubes small-celled infiltration may be seen, as in the squamous epithelioma, at certain points only, and these especially in the deeper parts of the growth. Small outlying nodules of the glandular tissue may also be observed.

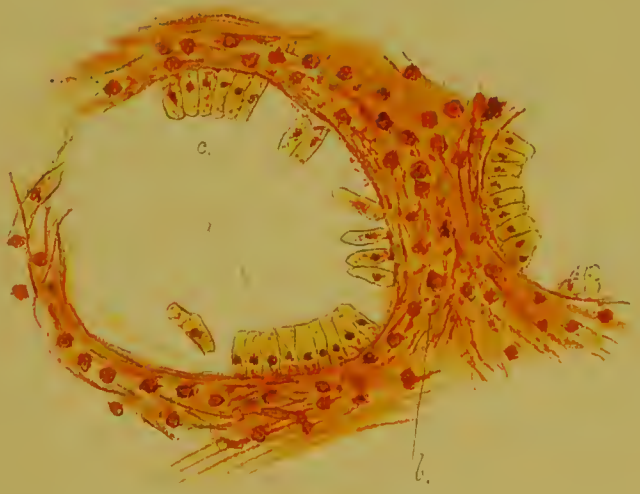


FIG. 119.—Columnar-celled epithelioma (adenoid cancer). Stained with picro-carmine. (× 300.)

a. Columnar epithelial cells.
b. Stroma in which are numerous young connective tissue cells.
c. The alveolar cavity.

Under a higher power the glandular tissue must be more fully examined. Each tube is found to be lined by a layer of regular

columnar epithelium, the nucleus usually being placed in the lower third of each cell. Beneath the well-formed epithelial cells flattened cells may, in very good preparations, be recognised, but they appear to be very inconstant even in number. Around some of the tubes, especially those near the surface, the stroma is like normal connective tissue, but in the deeper parts of the tumour, as already described, there is a great increase in the number of small round cells.

In the lung the appearances are much the same, the tubules invading the lung substance in all directions. The appearances described above under the high power are here very readily recognised.

In the liver, if a small piece of the pink peripheral part of the tumour be examined, the appearances are also very similar to those

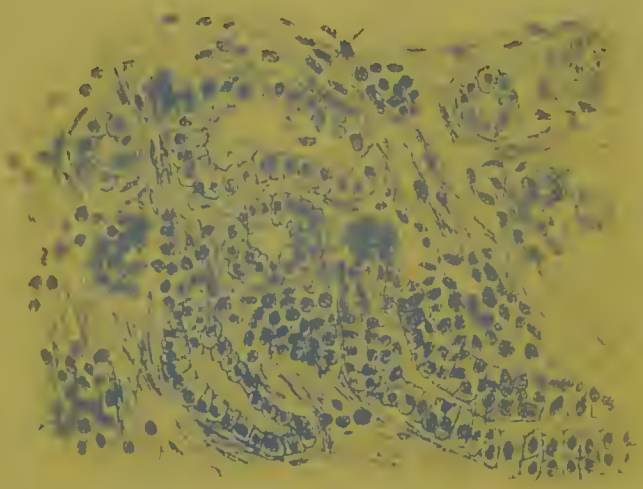


FIG. 120.—Columnar epithelioma. Secondary growth in the mediastinal gland. Stained with logwood. (× 300, after Greenfield.)

e.s. Single layer of epithelium in irregularly shaped space.
e.d. Double row of epithelial cells.
c.t. Young growing connective tissue cells (indifferent tissue).

before described; but if a portion taken from the central harder part be examined, an enormous increase in the stroma may be demonstrated. At the same time, this stroma is more fibrous, and the round cells are comparatively few in number. In consequence of this increase in the amount of stroma, the gland follicles or tubes are more widely separated, and are much more irregular both in size and shape, and where the tissue in the centre is still older, the epithelium filling the spaces becomes much more irregular, and the tubular arrangement is lost entirely. These points must be carefully kept

in view when the growth and development of malignant adenoma and its relation to true carcinoma are under consideration.

Carcinoma or Cancer.

283. The true carcinoma consists of a system of connected alveoli, bounded by fibrous walls, and containing cells of an epithelial type. Imbedded in the fibrous stroma, and quite separated from the epithelial elements, run *well developed* blood-vessels. If, further, it is stated that the alveoli are in direct communication with the lymphatics at the margin of the tumour, the essential features of the carcinoma are enumerated. Any classification given must depend (1.) upon the amount, nature, and arrangement of the stroma, and (2.) the number and character of the cellular contents of the alveoli.

Scirrhous Cancer.

284. In the scirrhous or hard cancer the typical carcinomatous structure is well developed. The stroma, with its well-formed blood-vessels, both derived from the mesoblast and the epithelial cells, derived most probably either from the epi- or hypo-blast. Its alveolar structure is exceedingly well marked, from the fact that the growth is slow, and the fibrous stroma is well developed. It occurs as a hard, firm tumour, varying somewhat in appearance, according to the position in which it grows—breast, pylorus, œsophagus, rectum, testes, ovary, kidney. In the breast it forms a hard, rounded tumour, which is firmly attached to the subcutaneous tissue, and very frequently causes retraction of the nipple, which is the least resistant point. The section has a greyish white glistening or silvery appearance, fibrous bands running across and between small yellow masses of fatty tissue. In the centre of the section the fibrous bands retracting cause a depression, whilst the fatty masses project slightly above them. Near the centre occur small patches of creamy or doughy tissue, and these are at once seen to be due to fatty degeneration of older portions of the tumour. Towards the periphery the tissue is much more vascular, assumes a more pink colour and a softer consistence. Take a scraping from the margin of the tumour. It consists of a milky fluid, which causes turbidity in water. Examined

under a high power (× 300), cells are found, irregular in shape when separated, generally smaller than ordinary epithelial cells, but with one or more distinct nuclei, and distinct nucleoli, the whole being surrounded by a cell wall. A scraping taken from the fatty centre is creamy and more opaque, and, examined under the microscope, presents small shrivelled angular cells, epithelial in type, but undergoing marked fatty degeneration: they are filled with small oil globules and granules.

Harden a piece of the peripheral part of the tumour in Müller's fluid (§ 53, p. 42), a second in methylated spirit (§ 52, p. 42) or picric acid (§ 61, p. 45), stain sections in picro-carmine (§ 73, p. 53), and mount in Farrant's solution (§ 98, p. 71).

Treat a piece of the central part of the tumour in the same manner.

Under the low power (× 50) examine a section from near the periphery. The tissue is seen to be composed of two sets of structures—first, the connective tissue series, stained pink or crimson; and secondly, the epithelial elements, which are stained brown or yellow (the nuclei pink). The connective tissue is so arranged that it

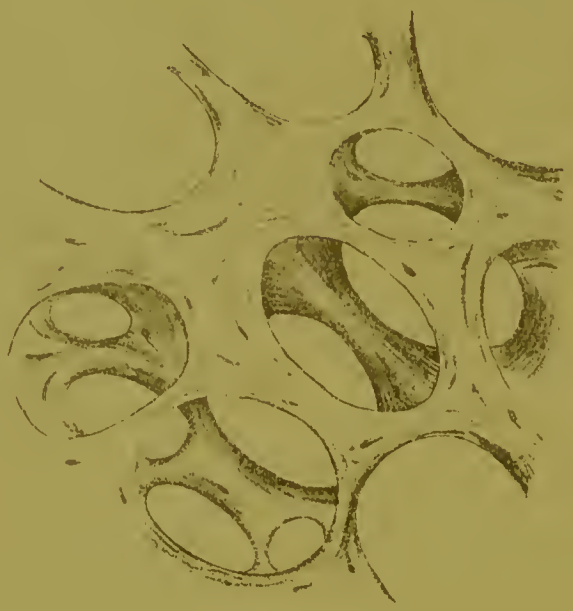


FIG. 121.—Stroma of cancer, lying in which are the alveoli, from which the epithelioid cells have been removed by pencilling. (× 300, after Cornil and Ranvier.)

bounds a series of rounded or irregular spaces, the alveoli in which the epithelial cells are collected. In this section the stroma is par-

tially fibrous and pink, but at certain points there are great accumulations of deeply stained cells. These occur most frequently near the margin of the tumour, and form the so-called indifferent tissue into which the epithelial masses project: wherever the stroma is young and growing, these small cells are present in considerable numbers. They are young connective tissue cells, and the extreme periphery of the tumour is made up entirely of this tissue. In these bands of stroma the well-developed blood-vessels are readily distinguished, and they are seen to be quite separated from the epithelial masses. Although the bands of stroma are well marked, they are not nearly so thick and dense as they are near the centre of the tumour. Even



FIG. 122.—Scirrhous cancer of the breast. Stained with picro-carmine. (× 50.)
a. Fibrous stroma, in which run well-formed vessels.
b. Alveolus.
c. Epithelioid cells.

under this power the alveolar spaces may be seen to be filled with angular cells, tolerably regular in shape, closely packed together.

Under the high power (× 300) examine the stroma more carefully; observe the pink fibrous and crimson cellular elements; note the position of the blood-vessels, surrounded by the fibrous bands; examine the indifferent tissue at the margin of the tumour, and observe that in it are no alveoli and no epithelial cells; and lastly, examine very carefully the angular cells which lie crammed together in the alveoli. The protoplasm is stained brownish yellow, but the

nucleus is deep crimson ; in this nucleus (or there may be more than one) nucleoli and vacuoles may be seen as deep crimson points and

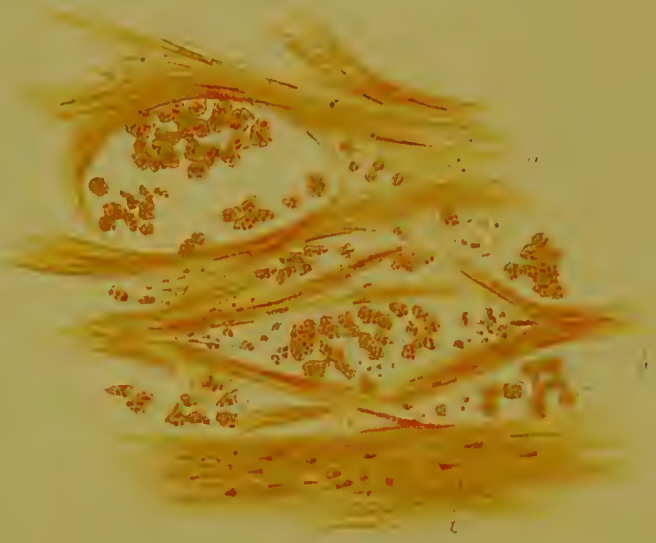


FIG. 123.—Scirrhous cancer of the breast. Stained with picro-carmine. (× 300.)

a. Fibrous stroma bounding
b. Alveoli.
c. Epithelioid cells, some with several nuclei. Note the irregular shape and epithelial character.

small clear spaces. There is no intercellular substance, or, at most, only a small quantity of fluid material.

To further examine the structure of the alveoli, and to determine their communication with the surrounding lymphatics, a thin section of the tumour taken from near the growing margin should be treated at once with nitrate of silver (§ 92, p. 67), and then mounted in glycerine. Examine as above.

Now examine the section from the central part of the tumour under both low (× 50) and high (× 300) powers. It may be observed that the fibrous stroma has become exceedingly dense, and in some parts constitutes almost the entire mass of the tumour growth. The alveolar spaces are much smaller than those already examined, and contain only a few shrivelled atrophied and angular cells. These cells have undergone fatty degeneration, and the greater part of them have evidently been absorbed, as the stroma becomes more dense, but less vascular. As the stroma comes to predominate more and more, it becomes more fibrous and cicatricial, and, like all cicatricial tissue,

tends to contract; and it is to the contraction of the tissue in this position that the central retraction or umbilication of the scirrhous cancer is due.

Encephaloid Cancer.

285. Under this heading come all those soft, rapidly growing brain-like or medullary cancers, in which the stroma is very scanty, the alveoli large, and the cells numerous. They may be primary tumours, growing especially from the mucous membranes, testes, and breast; but they also occur as secondary growths, following primary scirrhous cancer, the secondary growths in such cases becoming encephaloid, especially where the organ in which it occurs is vascular. They are seen as soft, pale pink nodules, of various sizes and shape, and, when scraped, a considerable quantity of the opaque cancer juice is brought away. Hæmorrhages are frequently met with in this tumour.

Harden a piece of the growth in Müller's fluid and spirit (§ 54, p. 43), stain a section in picro-carmine (§ 73, p. 53) and in Farrant's solution (§ 98, p. 71).

Examine under a low power (× 50). The pink stroma is exceedingly scanty, the vessels are relatively numerous, and, in consequence of the sparseness of the stroma, are badly supported, though they are usually well developed as regards their proper structure. The alveoli are very numerous, but vary greatly in size, and they, with their contained epithelial cells, constitute the greater part of the growth.

Under the high power (× 300) note that the stroma is very delicate, and in many cases excessively cellular, and that the blood-vessels are very indifferently supported. At some points there may be extravasations of blood from ruptured vessels, in which case the blood corpuscles find their way into the alveoli.

In the alveoli the cells stained brown present great differences, both as to size and arrangements. In some cases they are large, almost columnar cells, arranged regularly near the wall of the alveolus, but grouped indiscriminately near the centre, the arrangement here resembling that of the malignant adenoma. In others the cells may be large and rounded, having three or four nuclei and nucleoli, or they may be polygonal or irregular in shape. It may be stated generally that the shape and size of the cells vary according to the source

of origin of the tumour; when gland duct structure is the source, the cells are columnar; when the breast, they are like those which are found in developing acini.

The cells multiply by indirect division of the nucleus; a process which may be very readily followed in this position.

Colloid Cancer.

286. The colloid cancer must be looked upon as one of the already mentioned forms of cancer, in which there is a tendency of the epithelial cells to undergo colloid or mucoid degeneration. They are especially common in the gastro-intestinal mucous membrane, in the abdominal cavity, the breast and the ovary, and more rarely they are found in other viscera.

To the naked eye the presence of the colloid change is indicated by a peculiar brownish glue-like or gelatinous appearance. When the growth is diffuse, and occurs on a serous membrane, as in the peritoneal cavity, it may form a gelatinous mass, which appears as a coating for the whole of the abdominal organs, or like a gelatine cast of the viscera. Where the colloid change is present in cancer of the breast, it takes place in portions only; and these are indicated by the same peculiar gelatinous substance.

Treat as for the encephaloid cancer (§ 285, p. 441), and examine under the microscope. The pink stroma differs in no respect from one or other of the forms previously described; but under the low power (× 50) the alveoli are more rounded, and in place of cells there may be simply a yellow colloid mass.

Examine under the high power (× 300), and notice that where the cells are not entirely replaced by colloid, they are swollen, rounded, and contain drops of the yellow material in their protoplasm. In some cells the protoplasm forms a mere film around the colloid globule, and eventually even this disappears, and the colloid joins the main mass. In others a few altered and swollen cells may be left in the centre of the colloid, in addition to which, especially in the breast, the yellow gelatinous material may have penetrated between the layers of fibrous tissue forming the wall of the alveolus; and these, stripped off one after the other by the invading colloid material, give

rise to a peculiar laminated appearance around the alveolus ; first the altered cells in the centre, surrounded by colloid, external to which are successive layers of pink fibrous tissues and of colloid alternately.

Degenerative Changes in Cancers.

287. These changes may modify the appearances, both naked eye and microscopic, to a very great extent.

Colloid and fatty degeneration have been already mentioned. Myxomatous degeneration of the stroma sometimes occurs.

The tumours may soften *en masse*, or superficially, and so lead to ulceration, by a process of fatty degeneration or necrosis. This occurs especially when the tumour is exposed to the action of irritant or digestive fluids, or to mechanical injury. Such ulceration is usually followed by hæmorrhage. Hæmorrhage also occurs, as already mentioned, in encephaloid cancers, and it is frequently met with in *carcinoma telangiectodes* or erectile carcinoma, where well-developed vessels, on which are small dilatations, project from the stroma into the alveoli, and, being no longer supported, rupture, and give rise to serious hæmorrhage. Inflammation of cancerous growths is also very commonly found, and the results are very similar to those met with in inflammation of any normal tissue—as vascular changes and connective tissue proliferation.

Pigmentation of the stroma of cancerous growths also occurs, but it will be found that most of the so-called pigmented cancers are melanotic sarcomas.

After the description of the various forms of cancer, it will be understood that they are all of an exceedingly malignant character. The encephaloid is most malignant, the squamous epithelioma least so. They spread by lymphatics both locally and to distant parts. The following tabular form may prove helpful to the student who has carefully examined both the sarcoma and the carcinoma.

	Sarcoma.	Carcinoma.
1. *Origin* . .	Entirely mesoblastic.	Meso- and epi- or hypo-blastic.
2. *Stroma* . .	Intercellular. Does not form alveoli only.	Forms alveoli, which communicate with one another, and surrounds masses of cells.

	Sarcoma.	Carcinoma.
3. *Cells* . . .	Granulation tissue or embryonic cells, not epithelial (shape various).	Epithelial, shape and size various. Distinct nuclei and nucleoli.
4. *Intercellular substance.*	Present.	Absent, or merely fluid.
5. *Vessels* . .	Embryonic in character. In contact with the special cells of which the tumour is composed, and formed by modification of them.	Well developed, entirely contained in the walls of the alveoli. Not in contact with the cells, except in very rare cases.
6. *Spread* . .	By blood-vessels.	By lymphatics, except in the later stages, when they may also spread by blood-vessels, and then very rapidly.
7. *Malignancy*,	Great.	Greater.

CHAPTER XIII.

ANIMAL PARASITES.

Trematoda.

288. *Distoma hepaticum*, or *Fasciola hepatica* of liver-rot in sheep, occurs much more rarely in man. Found as flattened leaf-like worms, one-half to three-quarters of an inch long, lying curled up in the bile ducts and gall bladder. When flattened out the *D. hepaticum* is broader at the anterior than at the posterior end, but is prolonged into a narrow proboscis in front. They are brownish in colour, and through the brown a pink tinge may be seen. To inject the worm, kill by plunging it into a thin gelatine carmine, which is immediately taken into the alimentary canal. To preserve for examination soak thoroughly in glycerine, and mount in a deep cell in the same medium. With a hand-lens examine and note the oral sucker at the anterior extremity of the proboscis; from this runs the injected alimentary canal, which is deeply bifurcated and branched, giving off lateral diverticula, and ending in cœca. Behind the mouth is the genital aperture, and next to this comes the ventral acetabalum or disc; behind which again comes a convoluted tube, the uterus, occupying a considerable proportion of the body cavity. The testes are situated more centrally, and are bifurcated. The body is enclosed in a chitinous cuticle, covered with very minute spines. *Intermediate host*, fresh water snail; *cycle of generation*—ovum; ciliated embryo, set free in water by opening of operculum; embryo loses cilia and enters intermediate host, where it becomes encysted. It then forms sporocyst or redia form, by a process of internal gemmation, by which small tailed embryos are formed—the cercariæ; these escape, and enter the final host, after swimming in water by means of the muscular tail, and become sexually developed as hermaphrodites, and lose their tail.

D. lanceolatum also occurs in man.

D. hæmatobium, *Bilharzia hæmatobia*, or blood-fluke, is an important member of this group, as by its presence in the portal and splenic veins, and the vessels of the mucous membrane of the rectum and bladder, it gives rise to a condition of hæmaturia. It is met with especially in Egypt, the West Coast of Arabia, Mauritius, and the Cape. Unlike the other trematodes, it is bisexual.

The male is about half an inch long, is somewhat flattened and curved in on its ventral surface, so that a section is crescentic. Both discs, larger in the male than in the female, are placed near the anterior extremity, and the genital orifice lies behind the posterior of these. The female is about one inch in length, is filiform, and is received into the ventral groove, and a canalis gynæcophorus formed by a further folding in of the lateral margins at the posterior extremity of the male. In the urine from a case of such parasitism a quantity of blood may be found; but sometimes scarcely a trace of blood can be detected with the naked eye. If, however, some of the sediment be examined under the microscope, large numbers of ova may be distinguished. These ova are about $\frac{1}{180}$ of an inch in length, are oval, and have a spine or beak situated usually at the broader end. They are yellow, are transparent and smooth, and through the transparent investment may be seen the segmented yolk mass. If a few drops of water be added to these ova, and they are watched under a low power for ten or fifteen minutes, a movement of cilia may be observed within the investing membrane. This becomes very active immediately before the membrane ruptures. The released embryo has imperfectly developed organs, but darts about with great rapidity, the cilia working actively. They may be stained in picro-carmine, and mounted in glycerine, or, better, in Farrant's solution.

D. crassum, found in the duodenum; *D. sinense* and *D. conjunctum*, in the liver; *D. heterophyes*, in the intestines, are other important members of this group.

Cestodes or Tape-Worms.

289. Each so-called tape-worm is in reality a colony of slightly different individuals. Each segment or individual is sexually complete,

with the exception of those situated at the anterior extremity. The whole chain is termed a strobilus, the most anterior modified segment the head and neck ; after which come first the sexually immature, and next the matured, but hermaphrodite, segments or proglottides. In this group alternation of generation is strictly adhered to. The fully developed form occurs in the alimentary canal, and must be looked for in the fæces, to do which the fæces must be carefully broken down with a stream of water, and strained through fine muslin, so as to intercept the various fragments of the strobilus.

Tænia Mediocanellata, T. Saginata, or T. Inermis.

290. This is probably the commonest form in England and India, but in Germany it is not frequently met with. The intermediate host, in which the cystic form (*Cysticercus bovis*) occurs, is the ox, where it is found in the muscles, lungs, and liver.

The matured strobilus is a soft, flattened, yellowish white "band" worm, which sometimes attains a length of over twenty feet.

Examined under a low magnifying power, the head is seen to be square and somewhat flattened, about one-twelfth of an inch in diameter, having



Fig. 124.—Head and immature segments of *Tænia mediocanellata* (natural size).
a. Head with four suckers.
b. Neck.
c. Immature segments.

no beak or rostellum, or only a small proboscis, and without hooklets. At each corner of the head is a muscular sucker, and from each sucker runs a water vascular canal. In the centre of the head is a rounded opening, surrounded by the canals, into which the canals from the suckers open. From the circular canal two longitudinal branches continue, one down each side of the various segments.

Examine the fully matured proglottides, as they are arranged in a row. Small papillæ with central openings may be observed alter-



FIG. 125.—Flattened head of *Tænia mediocanellata*, with four suckers well seen. Neck becoming constricted. (× about 30.)

nating irregularly on each side of the riband, a little below the centre of the segment. Running down each side of the flattened segments, which are square, or longer than broad, is the branch of the water vascular canal, whilst at the front part of each segment runs a transverse connecting branch. By plunging the living worm into a solution of carmine, a most beautiful injection of the water vascular system may be obtained. The uterus is very much branched, the diverticula branching dichotomously. The testis consists of a convoluted tube placed in the anterior part of the segment, from which

leads a duct ending in a cirrus or penis, which may in some cases be seen protruding through the genital pore; close to this is the opening of the vagina. Near the posterior part of the segment are a couple of small vitelline glands. Each strobilus consists of three or four thousand segments, those sexually matured commencing at about the 450th from the head. The cystic form is seen in beef as small yellowish spots, which are especially numerous in the thin curved muscles of a round of beef. To preserve these worms for future examination, soak in glycerine and mount in a deep cell in Farrant's solution; or stain in logwood or carmine (§ 75, p. 58), clear up thoroughly with clove oil or turpentine (§ 96, p. 69), and mount in a cell in Canada balsam.

Tænia Solium, T. Cucurbitina, or T. Vulgaris.

291. This is the form which occurs most frequently in Germany.



Fig. 126.—Head, neck, and immature segments of *Tænia solium*. Stained with logwood and mounted in Canada balsam. (× about 30.)

a. Rostellum.
b. Double row of hooklets, the anterior appear to be the larger.
c. Suckers.
d. Immature segments.

The cystic form — *Cysticercus cellulosæ* — occurs in pork, where it gives rise to the so-called measly condition. A similar cystic form is

met with more rarely in man, in the subcutaneous areolar tissue, between muscles in the eye and brain. Like the *T. mediocanellata*, the strobilus is composed of head, neck, and proglottides. The worm is several feet in length, and consists of about 1200 segments.

Examine, under a low power, first the head, around which are four suckers arranged below a well-marked proboscis or rostellum. The proboscis is armed with a double row of hooks, the anterior of which are the larger; but all of them are considerably larger than the hooklets of the *T. echinococcus*. The water vascular system near the head is double, is similar to that met with in *T. mediocanellata*, and may be injected in the same manner. The segments are square, or are longer than broad; the uterus—or, more properly speaking, the ovary—has a number of lateral branches (seven to ten), which again subdivide, but not nearly to the same extent as in the *T. mediocanellata*. The cirrus genital pores, which alternate regularly, should also be examined. Prepare as for *T. mediocanellata*.

Bothriocephalus Latus, or Tænia Lata.

292. This cestode, which is frequently met with in Ireland, Holland, North-east Germany, Geneva, Southern and Eastern Russia, and on the shores of the Caspian Sea, probably has its cystic form in some species of trout which are especially common in the regions mentioned. The bleak, according to Dr. Fock, quoted by Cobbold, is possibly the intermediate host in the case of this parasite, which occurs in the Dutch Jews. The pike, eel, and pout are also mentioned as intermediate hosts. This tape-worm is the largest of the group occurring in man, and may be as much as twenty-five feet in length and from a half to one inch in breadth. The head is about $\frac{1}{25}$ of an inch broad, is club-shaped, slightly flattened, with no rostellum and no hooklets; and running down each side is a groove, which is very characteristic of this genus. Behind the head comes a thin neck, and the proglottides, three or four thousand in number. At first these are extremely narrow and short; as the segments become sexually matured (at about the 600th segment) they are broader and about one-eighth inch in length, but at the posterior extremity they are as much as one quarter of an inch in length, but are narrower.

The individual segments are not so much flattened as in the tæniada, but still the worm is flat and riband-like. They have a brownish tinge, but in the centre of each segment, or a little nearer the front on the ventral surface, is a pigment spot, at which point there is a distinct elevation, or thickening, in the middle of which is placed the genital pore. The pigmentation is due to the presence of numerous dark-coloured ova. The uterus lies in the centre of the segment, and is composed of a simple tube, which is so coiled up that it appears to be rosette shaped. On each side of the rosette shaped uterus may be seen small saccules, which represent the testes. The water vascular system is similar to that of other members of the group. For permanent preparations of the head or of the segments stain and mount as for *T. mediocanellata.*

Cycle of development of these forms.—Commencing with the sexually matured segments, proglottides are voided from the intestine; ova are discharged from, or escape from, these as they become disorganised. They are then taken up by the first host, generally from water, into the alimentary canal; here the ovum opens by an operculum, and the embryo, with its three pairs of hooks, emerges, increases in size, becomes vacuolated, the hooklets disappear, a chitinous cuticle is developed, and an imperfect water vascular system makes its appearance. The sac then becomes thickened at one point, invagination commences, until a double walled sac, open at one end, is formed. At the bottom of the sac, on the inner wall, hooklets are seen (if present in the tape-worm form), then elevations, which eventually form the suckers; this inner part of the floor, looking towards the mouth of the sac, is really therefore the head. All this takes place in the first host after passing from the alimentary canal, and while the worm is a parasite becoming encysted in the intermuscular septa. In some instances, as in the hydatid cysts to be afterwards described, a secondary or even tertiary internal budding takes place, so that in the primary cyst a great number of scolices, or undeveloped heads, may be formed. When the muscular tissue, with the contained encysted parasites—as measly pork—is taken into the alimentary canal of the second host, the cyst wall is dissolved by the gastric juice, the head becomes evaginated, attaches itself to the wall of the intestine, proglottides are developed behind it, and the cycle recommences.

Where man is the primary host, the "measles" are found in the positions before mentioned. A fibrous pseudo-cyst is formed around the cystic parasite, which may live for a considerable time. On the death of the scolex, however, the cyst becomes calcified, the contents undergo caseation and calcification, and the only evidences of the scolex left are the hooklets, which may almost invariably be found.

The Tænia Echinococcus.

293. The *Tænia echinococcus*, or the tape-worm of the dog, is important only as it gives rise to a cystic form in man, who is the intermediate host. It is a worm measuring about a quarter of an inch in length, one-half of the whole length being taken up by the terminal proglottis, which is the only one that comes to sexual maturity. The head is rather like that of the *T. solium*, but is smaller. It has a distinct rostellum, which is surrounded by a double row of hooklets, thirty or forty in number, similar in shape to those of the *T. solium*, but only about one-third of the size. Here, too, as in the *T. solium*, there are four suckers, which may readily be seen. There is a well developed water vascular system; the genital pore is placed a little behind the centre of the matured segment. The uterus occupies the greater part of the segment, and is filled with ova.

Hydatid Cyst.

294. The cystic form of the *T. echinococcus* occurs most frequently in the liver and peritoneum, but also in the lungs, spleen, heart, and pericardium, nerve centres and retina, kidneys, muscles, and subcutaneous tissues. In Iceland, according to Cobbold, "They are the cause of one-sixth of the annual mortality;" and in Switzerland, Southern Germany, and Australia (Victoria) they frequently occur, but much more rarely in England and Scotland. These cysts vary greatly in size and number, as they may be only the size of a pin's head, or they may grow to several times the size of the organs in which they are developed. In some cases they are single, but in others there are several in the same organ, or there may be numerous cysts occurring in several organs at the same time.

Examine one of the cysts. Before the organ is disturbed there is usually considerable bulging at the point where the cyst is situated (in the liver, most frequently on the upper surface of the right lobe). Carefully make a crucial incision into this bulging part. In this way a fibrous capsule is cut through, and the flaps formed by the incision may be reflected from the true cyst. This fibrous capsule or pseudo-cyst consists of new or compressed tissue, the new being the result of irritation, by pressure, of the connective tissue of the organ. The true capsule is now exposed; it is white and opaque, almost like boiled white of egg, and from its outer surface surrounding well lighted objects, such as a window, are reflected. Open the capsule and take out some of the fluid. It has a specific gravity of 1004 to 1013; gives no gelatinous or other precipitate with heat or nitric acid, and therefore contains no albumen. With nitrate of silver a white cloudy precipitate is formed, as there is about a half per cent. of common salt in the fluid. When the fluid escapes the membrane curls inwards; this is a very marked characteristic. If the fluid be set aside to settle in a conical glass, and some of the granular-looking sediment, mixed with Farrant's solution, be mounted in a shallow cell and covered with a cover-glass, a number of the scolices may be examined.

Under the low power (× 50) they appear to be about the size of millet seeds. Some of them are rounded, others more elongated, and have at one end a dark-coloured disc or zone. The body appears granular, and small suckers may be observed.

Under the high power (× 300) the structure of the scolices may be further defined: the circlet of hooks; the suckers placed somewhat laterally; the body containing the bright-looking globules and particles. A number of hooklets may usually be seen in this fluid, and these should be carefully examined in order that they may be recognised, even after the other contents of the cyst have undergone suppuration, or other degenerative changes. Examine a scraping removed from the inner surface of the cyst, mixed with Farrant's solution, and pressed between two glass slips. It is found to consist of a granular mass, in which are imbedded the scolices, similar to those described above. From this endocyst or inner layer of the hydatid membrane are developed the scolices, or where the primary cysts are of large size, secondary cysts. As these secondary cysts

grow, tertiary cysts may in turn be developed within them. These of course are observed during the naked eye examination.



FIG. 127.—*A*. Tænia head or scolex from hydatid cyst. (After Huxley, × about 300.)

a. Hooks.
b. Suckers.
c. Cilia in water-vessels.
d. Oval, strongly refractile particles.
B. Single hooks, more highly magnified.

The ectocyst, or thick white of egg-like outer layer, varies in thickness according to the size of the cyst. It is the curling inwards of

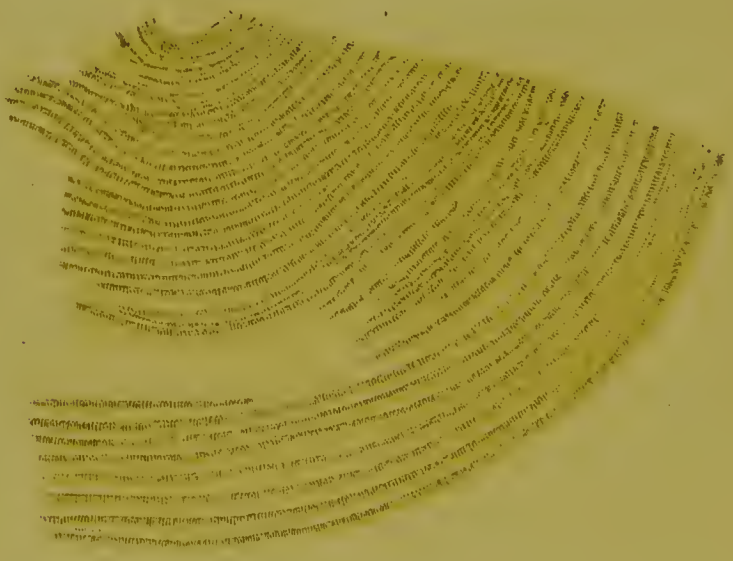


FIG. 128.—Laminated ectocyst of the true hydatid cyst. (× 300.) Note the pectinate markings on the laminæ.

this layer which causes the incurling of the membrane when the cyst is ruptured. With a couple of pairs of forceps it is possible to

strip layer after layer from the membrane, from which it is seen to be composed of a series of laminæ. If a small portion be teased out in glycerine and examined under the microscope, the lamination is easily made out; and on further examination under a high power each of these laminæ may be seen to be marked by a series of pectinate striæ running at right angles to the plane of the laminæ.

Degenerative changes which occur in the hydatid cyst:—

1. Spontaneous cure, due to absorption or evacuation of the fluid. This is followed by death of the scolices, fatty degeneration, caseation, and even calcification.

2. Evacuation after suppuration, or after inflammation of the surrounding tissues, in which there is marked softening of the membrane.

T. tenella (Cobbold)—cystic form, *Cysticercus ovis.* Mutton measles may be mentioned in this group, but it is unimportant; as is also *T. marginata* of dog—cystic form, *Cysticercus tenuicollis.*

Nematodes, Thread-Worms, or Round-Worms.

295. These are lumbricoid or filiform parasites, covered with a thick elastic cuticle. Some of them are found affecting man. They are bisexual, have a mouth, straight alimentary canal, posterior and ventral anus. Ovary in female, testis in male, more or less convoluted tubes in different species. Genital opening in female in middle, or even in front of middle, of ventral surface. Male cloaca, with or without spine, near the posterior extremity of the body.

The most important perhaps is the *Trichina spiralis*, which is met with in two positions,—one the mature form, in the intestine, the second the sexually immature form, encysted in the intermuscular connective tissue.

The Encysted Form of Trichina Spiralis.

296. The immature trichina, as is seen in muscle, either in pork or in the human subject, is usually found in the thin muscles of the abdomen, thoracic walls, diaphragm, cervical and laryngeal muscles, front

of the thigh, and less frequently the other parts of the muscular system. To the naked eye they appear as small whitish specks, longer than broad, lying in enormous numbers in the long axis of the muscular fibres.

Examined under a strong magnifying glass, the small specks are seen to be cysts, in which, coiled up, lie the larval trichinæ. Rupture the cyst with a couple of needles, turn out the trichina, and under the microscope examine the specimen, after staining with picro-carmine and mounting in Farrant's solution. It is about $\frac{1}{25}$ of an inch long, has an alimentary canal and imperfectly developed reproductive organs. Some of the white specks will be found to be quite hard and calcareous. If these are treated with hot caustic potash or soda, they remain unaffected, but a very weak solution of hydrochloric acid dissolves out the hard material and leaves the capsule soft and pliable.

Harden a piece of the trichinous muscle in Müller's fluid (§ 53, p. 42), cut sections (§ 67, p. 48); find a section in which is at least one cyst, stain with picro-carmine (§ 73, p. 53), and mount in Farrant's solution or stain in logwood (§ 74, p. 56), using Canada balsam (§ 96, p. 69) as the mounting fluid.

Examine under a low power (× 50). The cyst is seen to be placed between the muscular fibres, those in the immediate neighbourhood being somewhat compressed; it is lemon-shaped, and contains the larval worm rolled up in one, two, or three coils. At each pole, outside the cyst, a few fat globules, with small blood-vessels running through them, may be seen. The cyst itself is first fibrous, being derived from proliferated sarcolemma cells, and is stained pink. In the specimen from which the drawing was taken (Fig.), calcification of this fibrous covering is commencing at the poles (the dark portions). Where complete calcification has taken place, a fibrous covering is still often present. Within the first cyst is a second membranous or chitinous covering, which in turn may become calcified, whilst within this again is a quantity of granular protoplasm, in which the worm is imbedded. The complete calcification of the cyst is not completed for about ten months, after which, at an undetermined period, the contained larvæ may undergo fatty degeneration, and even calcification.

Examine more carefully under the high power (× 300), and corroborate the appearances above described. Cycle of changes.—When



FIG. 129.—*Trichina spiralis* encysted. Stained with picro-carmine. (× 300.)

a. Atrophied muscular fibres.
b. Fat cells situated at the end of the cyst.
c. Capsule becoming calcified.
d. Protoplasm surrounding the worm.
e. Trichina coiled up in the cyst.

trichinous pork is taken into the alimentary canal, the encysted larval form is set free by the action of the acid gastric juice. On the second or third day they become sexually matured. Both sexes are found. The adult male is about $\frac{1}{18}$ of an inch in length, and may be recognised by the two small processes in which the tail ends. The adult female is considerably longer, sometimes twice the length of the male; its body is longer, thicker, and the posterior extremity is "broad and bluntly rounded." The cloaca in the male is between the lobes of the tail, whilst in the female the genital orifice is placed at about the anterior third of the body. On the sixth or seventh day the female gives birth to numerous living sexually immature embryos,

which make their way to the muscular tissue, cause breaking down of the muscular fibres, and at the end of fourteen days are completely encysted, and then calcification ensues.

The following further list, selected from Cobbold's "Human Parasites," may prove of use to the student, in so far as it may serve as a guide in his search for descriptions of parasites.

Nematodes.

297. *Tricocephalus dispar*, or whip-worm.—A worm about two inches long; head and neck narrow, imbedded in mucous membrane of the cæcum; posterior two-thirds, thick, like whip-stock, curled in the male, straight in the female; anterior portion very thin; very common, but harmless.

Filaria sanguinis hominis—F. Bancrofti.—Found in blood in embryo form (*F. sanguinis hominis*), about $\frac{1}{150}$ of an inch in length, pointed at one end, blunt at the other. By their presence in the kidneys they give rise to chyluria and hæmaturia. In the fully developed form (*F. Bancrofti*) they are hair-like, about three or four inches in length, are met with in the lymphatics, especially those of the scrotum and lower limbs. Found especially in China, Australia, and Brazil.

Dracunculus or *Filaria medinensis—the Guinea worm.*—They may be from one to six feet in length, are cylindrical, and about one-tenth of an inch in diameter. They are found in the subcutaneous tissue of the back or legs, giving rise to swelling and subcutaneous abscesses, which burst, and the female parasites come to the surface. Found especially in India, Arabia, Guinea, West Indies, Egypt, Brazil, &c.

Eustrongylus or *Strongylus gigas.*—Found in the pelvis of the kidney of dogs and wolves and other fish-eating carnivora; only one case recorded in man. Male one foot long, female twice that length; body red, and about one-tenth of an inch in thickness.

Strongylus or *Filaria bronchialis*, a small species occurring especially in the lungs of sheep (rare in man). It is about one twenty-fourth the size of the large form.

Dochmius duodenalis or *Anchylostoma duodenale.*—Found in the duodenum and upper part of the intestine. The male is about three-

eighths of an inch long, the female half an inch. They attach themselves by their ventral mouth, situated near the anterior extremity, to the mucous membrane, from which they take blood, and by their presence cause extensive ulceration and hæmorrhage. Met with in cases of tropical anæmia in Northern Italy (St. Gothard Tunnel trichinosis), in the West Indies, Cayenne, Brazil, and Egypt.

Oxyuris or *Ascaris vermicularis.*—The small thread-worms, found in the cæcum and upper part of the colon, especially of children; the male about one-sixth of an inch in length, the female half an inch.

Leptodera or *Anguillula stercoralis.*—A small nematode found in the stools of patients suffering from Cochin-China diarrhœa. They are about $\frac{1}{25}$ of an inch long, and occur in very great numbers in the whole length of the alimentary canal, along with a much less numerous but larger form, the *L. intestinalis*, which is one-eighth of an inch long.

Ascaris lumbricoides or *Lumbricus teres hominis.*—Round-worm or maw-worm, found in man, pig, cat, and horse. Round worm with pointed ends. It is light brown in colour. Male four to six inches long, with curved tail, on which are two sharp spines; female ten to fourteen inches, tail straight, with no spines. Found in the upper part of the intestine, but they may be present in any part of the alimentary canal, in the bile ducts, and in the peritoneal cavity, and may be ejected with the fæces, or, more rarely, by the mouth.

Ascaris mystax or *A. alata.*—A small nematode, one-third of an inch in length, found in the alimentary canal of man, cat, dog, and other carnivora.

Acanthocephala, or Thorn-headed Worms.

298. One specimen, *Echinorhynchus gigas*, a quarter of an inch long, found in the small intestine of a boy.

Suctoria.

299. *Leeches* are not true parasites, and therefore need not be here described.

Arachnida.

300. *Pentastoma tænoides* of the nasal fossæ of the dog is the matured form of *P. denticulatum* of the liver, spleen, and kidney in man.

P. constrictum.—A larger pentastoma, infests the liver and lungs of man.

Acarus, or *Demodex folliculorum*, or face mite.—One of the mites met with in sebaceous follicles of the skin.

Leptus autumnalis, or harvest bug.—A small red mite which infests the skin, causing very irritable papules.

Acarus, or *Sarcoptes scabiei*, or human itch insect.—Found in tunnels in the deeper layer of the skin. The female burrows in the skin, laying her eggs as she goes, leaving a white track behind. The irritation set up gives rise to eczematous or vesicular eruptions. To obtain the acarus for examination the white line should be found, then the point of entrance to the tunnel, which is marked by a black speck, and the female is found at the opposite end. Cut down on to it with a sharp knife, place on a slide in a drop of Farrant's solution or glycerine, and examine. It is about "the size of a small pin-head, and somewhat turtle-shaped." On the under surface are four pairs of legs. The male is smaller (about half the size) than the female. The two anterior pairs of legs end in stalked discs, as do also the posterior of the two hinder pairs; the anterior of the hinder pairs end in long setæ. The female has both the hinder pairs of legs ending in setæ.

Insecta.

301. *Pediculus capitis*, or head louse.—Found on the scalp.

P. pubis, or crab louse.—Found on all hairy parts, except the head.

P. vestimentorum, or body louse, which lays eggs, and lives in the clothes.

Culex anxifer, or mosquito.

Glossina morsitans.—Tsetse of Africa, described by Dr. Livingstone.

Hæmatopota pluvialis, or clegge of the Western Highlands.

Cimex or *Acanthia lectularia*, or bed bug.—One of the "free parasites."

Pulex penetrans.—The jigger or chigoe of the West Indies. The female is found in the soles of the feet, beneath the skin.

Pulex irritans.—Common flea. Another of the "free parasites."

CHAPTER XIV.

VEGETABLE PARASITES.

Schizomycetes, or Bacteria.

302. In taking up the consideration of the schizomycetes, it will be necessary to depart from the general plan, and to give first a description of the methods employed in the detection of these very minute organisms, and then to give a short classification and description, as of the other parasites.

For examination of the schizomycetes unstained, in fluids they may be prepared according to Baumgarten's method, as given (§ 204, p. 297). Where, however, they are to be examined *in situ* in sections, the following method may be employed:—A fresh specimen, or one hardened in absolute alcohol (§ 51, p. 42), should be cut into a number of thin sections (§ 67, p. 48). As soon as the gum is washed out from the sections by warm distilled water, to which has been added a small quantity of pure carbolic acid, they must be transferred to a watch-glass, in which is some absolute alcohol, and left for a few minutes; then to ether; afterwards to a strong solution of acetic acid. Wash well in water, and transfer to a two per cent. solution of warm caustic potash or soda. By this treatment all fat granules, which may be mistaken for micrococci, all small crystals, which are sometimes mistaken for bacilli, granular looking fibrin, and even differentiation of structure, are removed, and only the resistant groups or strings of micrococci or bacilli are left for examination. Where there are masses of considerable size, with vessels or connective tissue spaces, this method is invaluable, especially for the removal of all elements which could be mistaken for micrococci or bacteria; and where there is any doubt at all in the mind of the observer, it should be

tried. Where, however, masses are absent, and where, although the presence of single micro-organisms is suspected, they cannot be distinguished, the method recommended by Koch should be adopted. This consists essentially in staining either the parasites alone, or the parasites and the nuclei, with a watery solution of some of the aniline colouring reagents. As adapted to the staining of tubercle bacilli, it has been already described (§ 200, p. 283).

For other bacilli—say the *Bacillus anthracis*—Weigert and Koch recommend the use of a saturated watery solution of gentian violet, methylaniline violet (ten minutes), methyl blue (thirty minutes), or Bismarck brown (twenty-four hours), in which the sections must remain until they are deeply stained; the time required for staining varies with the temperature and the reagent used. When deep enough in colour, they are washed for a few seconds in distilled water, then in weak acetic acid, and again in distilled water. If the

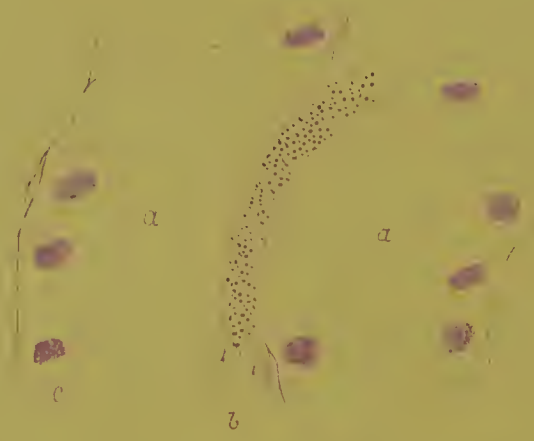


FIG. 130.—Micrococci in capillary vessel of the kidney, from a case of pyæmia. Stained with methylaniline violet. (× 650, after Coats.)

a.a. Tubules on each side of
b. Capillary blood-vessel filled with micrococci.
c.c. Nuclei of epithelial cells of tubules.

nuclei are to be left tinted, the section is at once mounted in Canada balsam (§ 96, p. 69), great care being taken that the sections do not remain for too long a time in either the alcohol or the clove oil. This method is exceedingly useful for the demonstration of the presence of micrococci. If the nuclei are to remain unstained, and the tissues cleared up to the greatest extent, the section is first stained as above,

washed in distilled water, and then transferred to a five per cent. solution of carbonate of potash, by which the colouring matter is discharged from all the tissues, but is left in the bacilli or micrococci. The

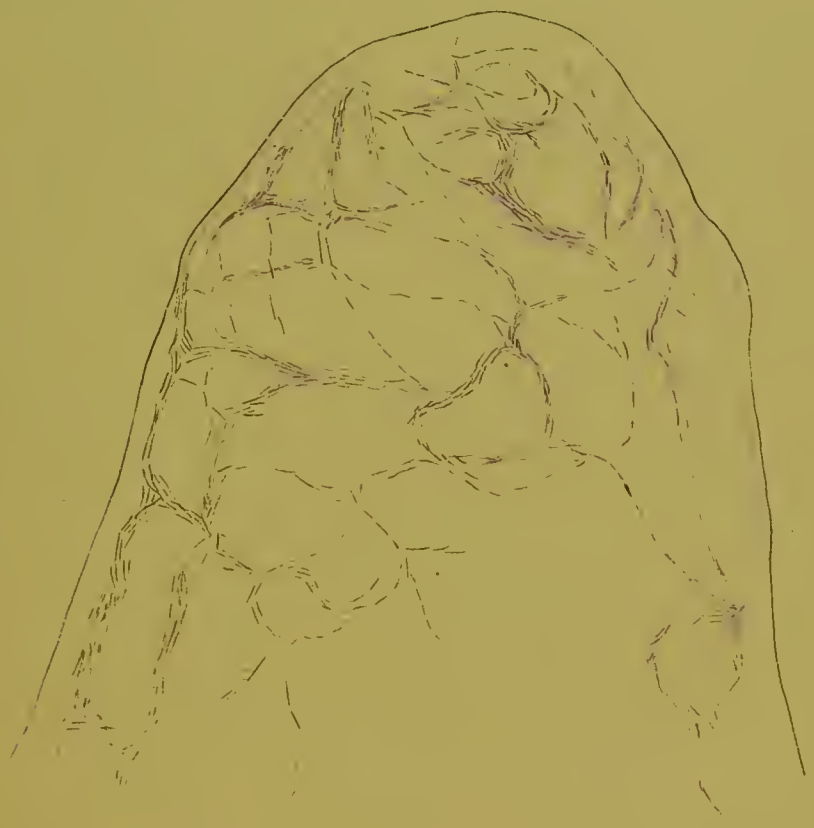


FIG. 131.—Villus of intestine of a rabbit, stained with methyl-aniline violet, cleared up with carbonate of potassium, and mounted in Canada balsam. (× 250, after Koch.)

The lines of bacilli corresponding to the course of the capillary blood-vessels are very readily followed in this specimen.

section is then mounted in either Canada balsam (§ 90, p. 96), Farrant's solution (§ 98, p. 71), or glycerine (§ 97, p. 70). This method is especially valuable for the demonstration and enumeration of bacilli contained within vessels or in thick sections, as in intestinal mycosis, where the anthrax bacilli are to be observed *in situ* in the capillary vessels of the intestinal villi. For pus, blood, and other fluids the so-called dry method is perhaps the most convenient for all practical purposes; it is essentially that already described for staining tubercle bacilli in sputum (§ 204, p. 298). The fluid to be stained

is smeared on a cover glass in a very thin layer, which is best obtained by pressing two cover glasses together. The glass with the thin film is held with a pair of forceps, and passed rapidly over a spirit lamp or gas flame—the smeared surface away from the flame—until the film is dry and the whole of the albumen in the stratum is coagulated. In doing this the glass should first be held at some distance from the flame, and then passed thrice rapidly through the flame, great care being taken not to scorch the layer. It may be stained at once, or, if carefully protected from external influences, it may be left for some time. Stain with some of the fluids previously mentioned, placing the cover glass, smeared side down, in the fluid; wash in distilled water, again dry carefully, and mount at once in Canada balsam, or clear up in alcohol and clove oil and then mount. It may be mentioned that although Canada balsam is most frequently used for preserving these bacilli, Farrant's solution and glycerine are both excellently adapted for this purpose, especially in the case of sections of tissues and of tubercle bacilli.

In connection with the manipulation of sections and fluids in which the presence of bacteria is suspected, it must be remembered that the greatest cleanliness is requisite—not only apparent but absolute; and to obtain this absolute cleanliness the apparent must first be attended to. No spot or blemish of any kind should be seen on any of the instruments used; the point of the knife or the platinum needle which conveys the fluid must be carefully polished; the cover glasses and slides must be carefully washed with acid and then with distilled water, the watch glasses and other utensils treated in a similar manner, and the whole carefully heated to a temperature above that at which organisms can exist—150° C. This is most easily done by passing them carefully through the flame of a spirit lamp, though it is very convenient to have a hot chamber in which the various utensils may be kept when not in use.

Method of examining the Preparations in which Micro-Organisms are supposed to be present.

303. Some of these organisms are exceedingly minute, and it is only with the greatest care, and with the aid of most perfect illuminating

apparatus, that a number of them are to be recognised. When once their presence is determined, however, their position in the tissues must be recognised, which can be done only by modifying the light and other conditions. Use an oil immersion lens—(those made by Zeiss are the best)—and an Abbe's illuminator, with which the best optical combination is obtained. The condenser has a very short focus, and must therefore be brought almost up to the under surface of the glass. It may now be used as an ordinary condenser, if the lateral or greatly converged rays be cut off by means of a diaphragm, with a small aperture placed below. If a large aperture in the diaphragm be used, the greatly converged rays of light are also allowed to play on the structures, which are lighted from all points, all shadows are lost, and the "structural picture" is lost. As the structural picture is lost, however, the stained elements, such as the micro-organisms, and the nuclei, are brought out prominently, and can be carefully examined. All preparations should be examined with both the small and the large apertures beneath the condenser. With the small aperture the structural elements are observed, and the positions of the organisms; as the apertures are increased in size,



FIG. 132.—Drawings of blood corpuscles and bacilli stained with methylaniline violet, and mounted by dry method in Canada balsam. (× 700, after Koch.)

A. White blood corpuscles, from one of the veins of the diaphragm of a septicæmic mouse. All stages of transition are shown, from blood corpuscles which contain but few bacilli, to those which have become converted into masses of bacilli.

B. Coloured blood corpuscles of septicæmic mouse, between which are seen the small bacilli.

C. Coloured blood corpuscles of a mouse affected with anthrax. The large bacilli are seen lying between the corpuscles.

the organisms become more and more prominent, whilst the structural elements gradually disappear from view.

A specimen of blood from a septicæmic mouse, prepared as above, examined under ordinary conditions, appears to contain nothing but white and red blood corpuscles. When, however, it is illuminated by means of an Abbe's condenser, and examined under a power of × 700, a number of exceedingly minute, deeply stained, rod-like bodies may be seen lying between the red blood corpuscles, or imbedded in the protoplasm of the colourless corpuscles. These are about the smallest bacilli yet described.

A specimen of blood taken from the spleen of a mouse, inoculated with anthrax virus, and examined in the same way, is seen to be charged with much larger jointed, purple, rod-like bodies, which are recognised as anthrax bacilli. Typhoid bacilli are recognised in the same way in a scraping from one of the enlarged soft mesenteric glands.

A drop of pus from an acute abscess, similarly treated and examined, presents numerous minute rounded bodies, either in chains or in zoogloœa masses, and some elongated or rod-shaped bodies lying free in the fluid, whilst in the pus corpuscles similar organisms are frequently imbedded, and can be readily observed.

Examine a section from a case of diphtheria, either of a cervical gland or of the uvula, especially its posterior surface, treated by the caustic potash method (§ 94, p. 68). Wherever there are micrococci in the zoogloœa form, they may be seen as small granular strongly refractile layers or masses, arranged on the surface, or contained within the lymphatic spaces, or in the gland follicles near the surface.

Stained with methylaniline, they are seen in the same positions, but they are then of a deep blue violet tinge. Living micrococci and bacilli are stained deeply, but when they become disorganised, like all dead tissue, the granular *débris* often stains very imperfectly, even though it is composed largely of broken-down micro-organisms. This fact must always be borne in mind, for, although stained organisms may not be present in large numbers in caseous or purulent material, a section taken from the wall of a caseous abscess may be swarming with masses which readily take on and retain very tenaciously, aniline colours.

Classification of the Schizomycetes.

Sphærobacteria.

(*a.*) *Micrococcus and* (*b.*) *Sarcina.*

304. The micrococci offer the smallest and most elementary form of vegetable organism. They are probably divided into cell membrane and cell contents. They may be isolated, as in the pyæmia of rabbits; in chains, as in the gangrene produced by inoculation in the house-mouse or field-mouse; or in zooglœa masses, united by a glue-like material, as in diphtheria; in the lymphatics in acute pneumonia; and in the spreading abscesses of rabbits, as described by Koch.

They may vary considerably in size and shape, the smallest being rounded and found in the spreading abscess above mentioned, whilst a larger, more oval form is met with in the septicæmia of rabbits. They appear to increase in number by a process of fission. When in large masses, they may be characterised by certain differences of appearance, generally manifested in the colour; for instance, some of them form brown colouring matter, others white, yellow, pink, red, blue, grey blue (as seen in blue pus), green, and the rest. Some of these may be obtained by exposing a boiled potato to the air for some time, when they grow as different coloured patches, any of which may be transplanted to a similar soil, where they grow and give rise to patches of colour similar to those from which they were taken. When examined under such conditions, they are found to be mixed with bacterium, termo, &c. (to be spoken of immediately).

Pathogeneous micrococci, or those which are supposed to be the cause of diseased conditions, are met with in the specific infective diseases.

In *diphtheria*, they occur on free mucous surfaces, in lymph spaces, &c. (see § 218, p. 327).

In *septicæmia*, they occur in connective tissue spaces; but also in capillary vessels at the points of junction between the arterial and venous capillaries, where the blood is flowing most sluggishly through the widest area, and where consequently the micrococci are most at rest as in the glomeruli of the kidney and in hepatic capillaries of the liver.

In *pyæmia*, as in the case of rabbits, the micrococci are found in similar masses in the vessels.

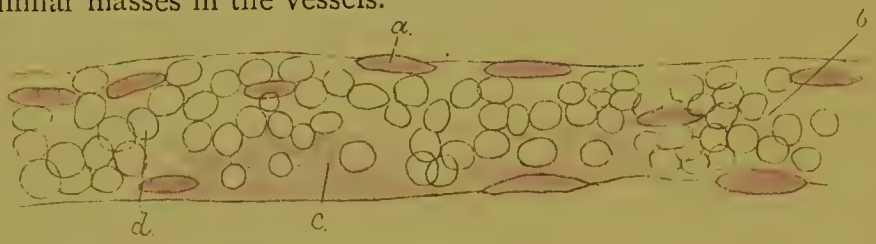


FIG. 133.—Vessel from the cortex of the kidney of a pyæmic rabbit. Stained with methylaniline violet. (× 700, after Koch.)

a. Nuclei of the vascular wall.
b. Small group of micrococci between the blood corpuscles.
c. Dense masses of micrococci adherent to the wall and enclosing blood corpuscles.
d. Pairs of micrococci at the border of the large mass.

In *purulent inflammations*, they are usually found either in the connective tissue or on mucous surfaces.

Erysipelas.—In chains or masses, which are found in the lymphatics and connective tissue spaces.

Puerperal fever, *scarlatina*, and *measles.*—In the blood, breath, and tissues.

Endocarditis.—See § 139, p. 146.

Acute necrosis and *infective myositis.*

Small-pox and *chicken-pox.*—In the vesicles.

Acute yellow atrophy.

In *croupous pneumonia* micrococci have been described, and have been cultivated in rabbits and other animals from fluids taken from a case of acute pneumonia.

Similar micrococci are described as present in acute catarrhal pneumonia.

Fowl Cholera.—According to the researches of Toussaint and Pasteur characteristic micrococci are present in this disease.

Sarcina.

305. Especially sarcina ventriculi, which is frequently met with in acid watery vomited matter from dyspeptic patients, in which the typical wool-sack formation occurs; the fission taking place so as to form masses of fours of small round micrococcoid organisms. A smaller form is met with in the lungs, pharynx, and urine. It has a green tinge.

Microbacteria.

306. These are the short rod-shaped bodies with rounded extremities, which are found in putrefying matter and dead tissues.

Bacterium termo is a minute rod-shaped body, varying from 0·5 to 1·5 micromm. in length. They occur in pairs or in zoogloœa masses, in which the gelatinous material is present in large quantities, they are essentially the bacteria of putrefaction.

B. lineola is like the above, but larger (3·8 to 5 micromm. in length). It may be found in various infusions, and may be cultivated on potatoes. Both these may be more or less active.

Desmobacteria.

307. Riband or thread-shaped organisms, which appear at some stage of their existence to be composed of strings of short rods. The strings may be composed of two or three segments only, or there may be a considerable number in each chain, whilst in some cases again, or at certain periods in the life history, the long filament is present, but it is quite unsegmented. The most important of these are—

The *Bacillus anthracis* of splenic fever, malignant pustule, charbon, and intestinal mycosis, is from 4 to 20 micromm. in length, and is about 1·5 micromm. in thickness. In the serous fluid thrown out in such cases into the pleura the rods are as much as 150 micromm. in length (these may have grown after the death of the patient).

This organism is found, especially in capillary vessels, at the points where the blood flow is most retarded. It may be present in such quantities as to cause plugging, distention, and rupture of the viscera, especially of the abdominal and thoracic viscera. Like the other members of the group, it commences as a spore, which elongates to form the rod-shaped bacillus. Under favourable circumstances this attains to as much as ten or more times the original length of the bacillus; the protoplasm of which it is composed becomes granular; highly refractile spores are formed in this at regular intervals; after which the thread breaks up into lengths, the spores are set free, and the same process again commences. In place of this series of

changes the bacilli may undergo simple division, especially in the blood of the living animal, as in splenic fever and in septicæmia of the mouse.—(Koch.)



FIG. 134.

A. "Wall of cavity in case of phthisis, showing the epithelioid tissue between the caseous mass and the inflammatory tissue, —bacilli in the epithelioid cells resembling somewhat the appearance of the bacilli in leprosy as regards their arrangement." (× 330, after Watson Cheyne.)

B. Tubercle bacilli, apparently with spores. (× 2,350, after Watson Cheyne.)

Bacillus tuberculosis, already described (§ 204, p. 298), which requires special staining.

Bacillus lepræ, which stains with most of the aniline colours, but not with Bismarck brown; it is 4 to 5 micromm. in length, and is imbedded in the cells of the nodules found in leprosy.

Bacillus of typhoid fever (§ 221, p. 332), in which, as in the *B. lepræ*, are small rounded or oval bright unstained spots, which may be either vacuoles or spores. Two forms; long and short rods in the ulcers, and short rods in the spleen, kidney, liver, and blood.—(Koch.)

Bacillus of septicæmia (of mice), ·8 to ·1 micromm. in length, and about ·1 to ·2 micromm. in diameter (§ 304, p. 467).

Bacillus of erysipelas (of rabbits), 3 to 10 micromm. in length, and ·3 micromm. thick, which occur in tufts or clumps on the surface of the ear cartilage of the rabbit in erysiplas; induced by inoculation.

Bacilli of purpura hæmorrhagica, which may be stained best with methyl-blue, have recently been described as present in certain positions in the small vessels of the pericardium (W. Russell and Watson Cheyne). They are exceedingly small, and appear at first sight like micrococci, but they are true bacilli. In connection with this organism

it must be remembered that micrococci have been already described as present in "Hæmophilia neonatorum."

Bacillus malariæ.—Found in the air of malarious regions, and in the blood in the cold stage of ague, and in the blood and spleen of patients who have died of malarious fever. It is described as a rod-shaped bacillus, in which spores, single or in couples, may be seen. These rods may be found in the blood corpuscles.

Bacillus of syphilis is also described as occurring along with micrococci in hard chancres; and bacilli are similarly found in farcy.

Spirobacteria.

308. Spiral or screw-shaped organisms, of which the most important is the spirillum or *Spirochæta Obermeyeri*, which is found in the blood in relapsing fever. It must apparently be examined in the fresh condition, as it rapidly breaks down, even in such an innocuous fluid as distilled water. Examined in the living blood on a warm stage, it is seen as a very active spiral organism, which is usually two, three, or four times the length of the diameter of a coloured blood corpuscle.

309. For the Method of Cultivation of Bacillus Anthracis

See Koch, zur Untersuch d. Pathog. Organ., p. 24, or Mittheil, a. d. kaiserl Gesundheitsamte, Berlin, 1881, &c.

See Klein in Report of the Local Government Board, 1881-2, p. 172, *et seq.*

310. For Method of Cultivation of Bacillus Tuberculosis

See "Koch, Berlin Klin Woch," 15, 1882. See also "Nature," May 4, 1882, to which papers those who wish to study the development of bacilli are specially referred. Although this branch of pathology is now coming into great prominence, the subject is so wide and the methods of manipulation are so delicate and intricate that the student requires to make a special study of the subject, and in the space at command only directions the most incomplete, and therefore liable to be misleading, could be given. It may be mentioned that Dr. Heneage Gibbes quotes methods for the cultivation of bacilli in his "Practical Histology and Pathology."

Hyphomycetes, or Moulds.

311. The most important are—

Achorion schonleinii (favus fungus, forming the yellow cup-shaped masses around hairs) which is found in the root sheath of the hair

bulb, in which the jointed hyphæ or rod-shaped filaments, with clear globules within, and rounded spores or groups of spores (conidia) may be found amongst the epithelial cells. It is best prepared by staining in methylaniline violet, washing carefully in distilled water, and mounting in glycerine. It may also be soaked in water, and treated with caustic potash or acetic acid, or it may be treated with a mixture of alcohol two parts, ammonia one part, and mounted in distilled water.

Tricophyton tonsurans, *Tinea tonsurans*, or ringworm, prepared in the same manner, is seen in the form of slender jointed rods and small highly refractile spores; these spread not only into the sheath, but also up the shaft of the hair.

Microsporon furfur of *Tinea* or *Pityriasis versicolor* occurs as yellowish or brownish red patches, covered with thin scales. Scrape off a few of these scales with a knife, treat as before, and examine under the microscope. It is seen as thin curved filaments, the conidia are grouped into masses, whilst the short spore-bearing filaments form a dense network.

Actinomyces.

312. Actino-mycosis is a disease which was long mistaken for tuberculosis, and for other forms of new growth, such as osteo-sarcoma. The fungus itself appears as a rosette-shaped mass, with a central mycelium, from which radiate the conidia or club-shaped masses. As these grow they set up around themselves a proliferative irritation, by which a structure similar in most respects to that of tubercle is formed. Some of these masses, especially those of rapid formation, suppurate, giving rise to abscess cavities and fistulæ, from which a pus containing the actinomyces, "small white or yellow greasy looking masses lying among the purulent detritus," is discharged. It may be recognised with the naked eye, but much more readily under the microscope. In cattle the masses do not break down nearly so readily as in man, and sections of the tissues containing the fungus are easily made after hardening in absolute alcohol. (Stain in Spiller's blue, and mount in Canada balsam. The fungus remains unstained.) The nodules are usually of considerable size;

and when this is the case, they are found to be made of several or numerous follicles, as in tubercle. The masses may reach the size of the fist.

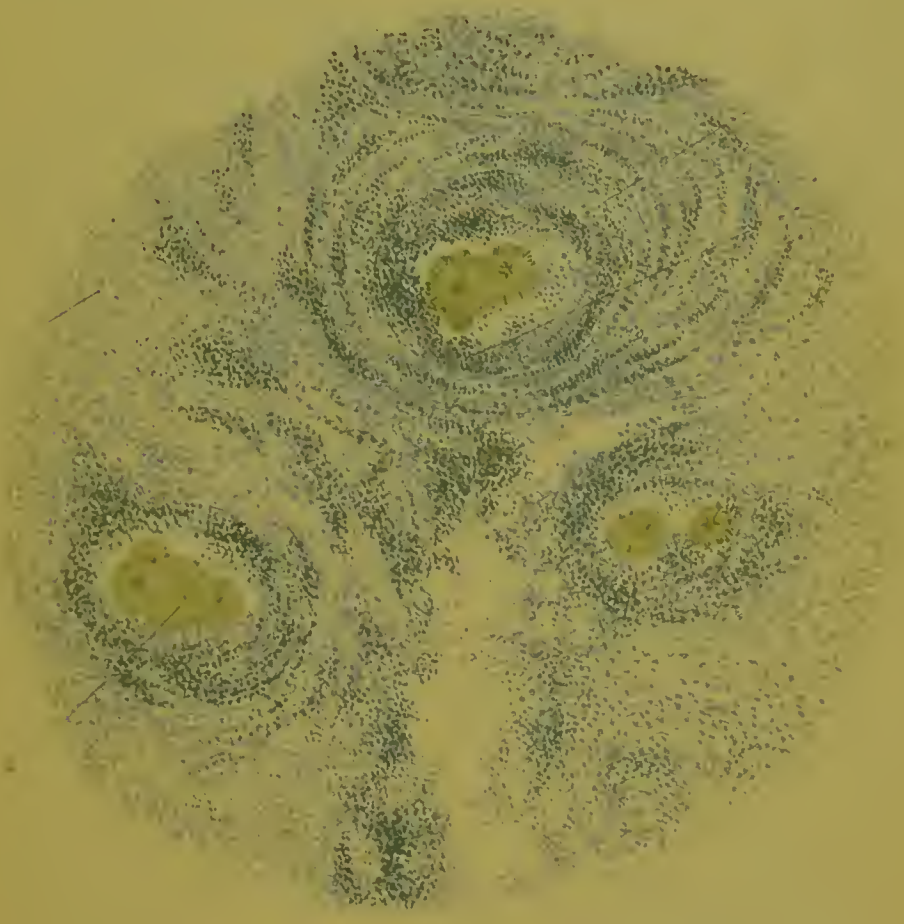


FIG. 135.—Fibrous nodule from a case of actino-mycosis (from the tongue of a cow). Stained with Spiller's blue. (× 50.)

a. Fungus growing in the centre of a follicle.
b. Large endothelioid cells near the fungus.
c. Fibro-cellular tissue away from the centre of the follicle, in which round cells predominate.
d. More fibrous tissue, still further from the fungus, forming a fibrous capsule.

The granulation tissue, endothelioid cells, fibrous bands, and the rest may all be distinguished under both low (× 50) and high (× 300) powers, as in tubercle.

In cattle the positions in which the disease most frequently occurs are lower and upper jaws, and first part of the alimentary canal; in

the human subject the soft parts of the neck, the mediastinal tissue, and the lungs.

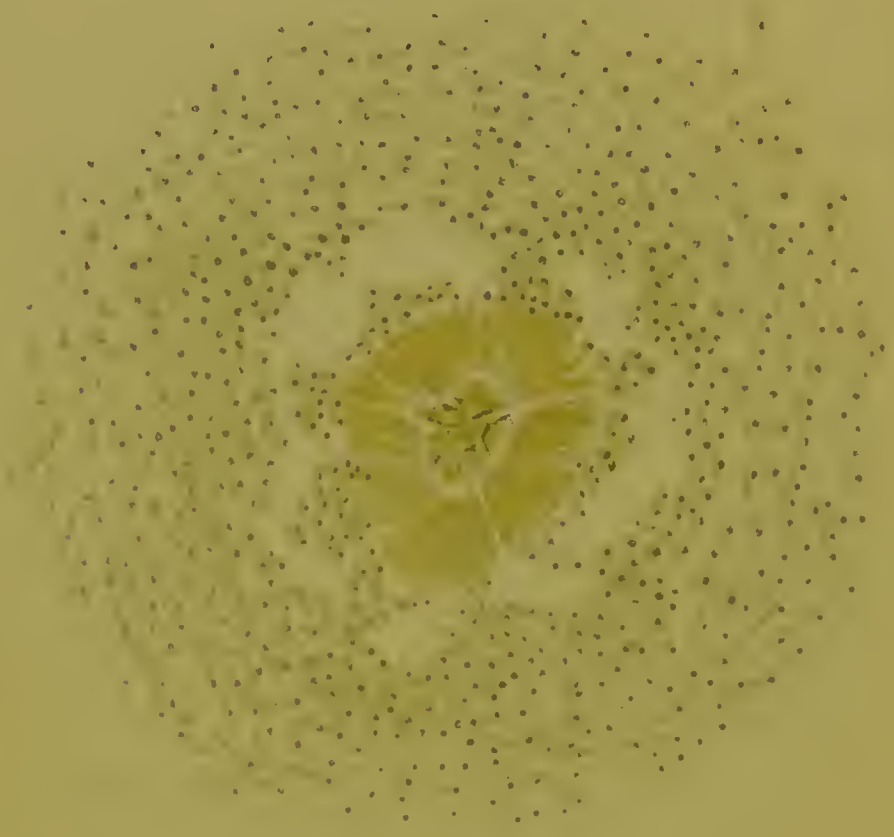


FIG. 136.—Actino-mycosis. Tongue of cow. Section stained in Spiller's blue. (×300.)

a. Centre of mass of conidia (conidiophore).
b. Pear-shaped conidia.
c. Endothelioid cells. (Compare these with the cells seen near the centre of a tubercle follicle).
d. Fibrillar tissue near the margin of the follicle.
e. Spindle-shaped cells, seen especially near the margin.

BLASTOMYCETES, OR YEASTS.

313. *Mycoderma vini* is said by Grawitz to be the parasite present in the white "thrush" or aphthous patches. He holds that multiplication in the so-called *Oïdium albicans* is by gemmation and abstriction, as in the true yeasts; with this exception the yeasts are, pathologically, quite unimportant.

ADDENDA.

Eosinated Hæmatoxylic Glycerine.

This reagent, as recommended by J. Renaut, appears to be specially useful for staining specimens hardened in chromic acid compounds, or in osmic acid, which are not well stained by carmine and picro-carmine. It is a differential stain, which in many respects is equal to picro-carmine.

The protoplasm of muscular tissue takes on the eosine, and is coloured a bright rose, the nuclei a deep violet; red blood corpuscles are stained brick red; axis cylinders of nerves are stained violet.

Prepare the solution as follows:—Take 300 grammes of neutral viscid glycerine, and saturate it with potash alum, gently warming the solution, and then allowing it to cool. To this add, drop by drop, a concentrated watery solution of eosine, until a slight opacity makes its appearance.

If a deeper eosine stain is required, it may be obtained by mixing ordinary glycerine, saturated in the same manner, with the alum saturated solution, until the required tint is obtained. Filter by means of an exhaust filter through fine paper, supported by well pierced parchment paper. This fluid should have a rose colour by transmitted light, and a peculiar fluorescent yellow green by reflected light.

To this solution again add, drop by drop, a concentrated solution of extract of hæmatoxylin (hæmatoxyline of Renaut) in alcohol, gently warmed and shaken until the saturation is complete.

The alcoholic solution of hæmatoxylin should be added to the eosinated glycerine until the mixture becomes a "beautiful violet purple," but still retains the green fluorescence. Should the fluorescence disappear, more eosinated glycerine must be added, until the green colour is again distinctly seen. Filter, and keep in flasks covered with paper, pierced with a pin. "At the end of three or four weeks, when all smell of alcohol has disappeared, filter again as above, and preserve the fluid in stoppered bottles."

Sections hardened in chromates are stained in from five to ten minutes, but those hardened in osmic acid require a longer time—one to six hours. The fluid may be used as a mounting fluid, the cover glasses being held in position by Canada balsam, or some other cement.

Sections may also be mounted in Canada balsam, if they are first washed in a weak, watery (distilled) solution of eosine, and then are cleared up in eosinated alcohol and oil of cloves, in which one per 1000 of eosine has been dissolved.

Specimens hardened in osmic acid in some cases become blackened after a time, but the violet and rose colours may be brought back by passing under the cover glass a drop of formic glycerine—$\frac{1}{200}$. When this is attained, the formic glycerine is replaced by hæmatoxylic glycerine, either pure or mixed with eosinated glycerine, if the rose colour is not deep enough.

Hæmatoxylic glycerine is prepared by adding a saturated solution of "hæmatoxyline" to glycerine saturated with potash alum, as before described. When the required strength is attained, the liquid should still be quite clear, and on being mixed with water no violet granules should be precipitated. If these appear, add a little more of the glycerine. Filter, and then treat as for the eosinated hæmatoxylic glycerine. It is a very good and clean logwood stain.

Bismarck Brown.

This staining reagent may be used as a glycerine (two to four per cent.) solution. Heat the aniline brown with glycerine in a test tube, allow this to cool, stain the section for a couple of hours or more, wash well in distilled water and mount in Canada balsam. It will be found of great advantage to allow the section or dried fluid to remain for a few minutes in a weak solution of carbolic acid before staining it.

Examination of Fungi, &c.

For the examination of fungi, aspergillus, &c., the following method will be found to be of great value. Into a watch-glass pour a mixture of absolute alcohol two parts, liquor ammoniæ one part.

Allow the fungus to remain in this for two or three minutes, and then transfer to a slide on which is a drop of distilled water, or glycerine if it is wished to keep the specimen as a permanent preparation.

Ether and Chloroform.

These fluids are especially used for dissolving out fat from tissues. When these are fresh it is necessary to drive out the water by means of absolute alcohol, as the fat is protected from the action of the ether or chloroform by the water.

Place the section in a watch-glass containing absolute alcohol, until all the water is removed, which will be the case if no milkiness makes its appearance, when the section is transferred to a vessel containing ether or chloroform. Allow it to remain in one of these fluids for a few minutes, and transfer first to alcohol, and then to a weak solution of acetic acid; stain and mount as for other sections.

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